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Development of Natural Crude Drug Resources from Taiwan (V)[1] Pharmacognostical Studies on Chinese Crude Drug "Peh-hue-juwa-chi-chhau" (白花蛇舌草) (1)

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"Peh-hue-juwa-chi-chhau" (白花蛇舌草), very important folk medicine in Taiwan, has been used as an anticancer, antitoxic and diuretic agent, in the treatment of cancers, appendicitis, enteritis, hepatitis, eye diseases, contusion, furunculosis, bleeding etc. There are many varieties of "Peh-hue-juwa-chi-chhau" found on the Taiwan market. To clarify the botanical origins of the commercial drugs, histological studies were made. From the characteristics of the external structures of the materials, it is found that "Peh-hue-juwa-chi-chhau" is derived from the entire plant of the following species: (1) *Hedyotis diffusa* WILLD. (2) *H. corymbosa* LAM. (3) *H. tenelliflora* BLUME. (4) *Mollugo pentaphylla* L. The study on the other comparative *Hedyotis* spp. and *Mollugo* plants will be reported in the next paper. The morphological characteristics of "Peh-hue-juwa-chi-chhau", *Hedyotis diffusa* WILLD., *H. corymbosa* LAM. and *H. tenelliflora* BLUME from Taiwan are shown in TABLE I.

Keywords——*Hedyotis* spp.; Peh-hue-juwa-chi-chhau; Rubiaceae; Taiwan folk medicine; botanical origin; plant anatomy

"Peh-hue-juwa-chi-chhau" (白花蛇舌草), very important folk medicine in Taiwan, has been used as an anticancer, antitoxic, antipyretic, and diuretic agent, in the treatment of cancer, enteritis, hepatitis, appendicitis, eye diseases, contusions, furunculosis and bleeding *etc.*

"Peh-hue-juwa-chi-chhau" was believed to be derived from the whole herb of *Hedyotis diffusa* WILLD.[2] of Rubiaceae by Kan,[3] Hsu,[4] Kao.[5] However, it has not been proved. Besides, many varieties of goods on the Taiwan market which take this name are different from the plant. Judging from their appearances, they seem to be derived from *Hedyotis* spp. of Rubiaceae and *Mollugo* sp. of Mollugiaceae.

The purpose of this paper is to clarify the botanical origins of "Peh-hue-juwa-chi-chhau" on the Taiwan market, by histological studies and compared it with *Hedyotis* and *Mollugo* plants found distributed in Taiwan.[2]

The research about "Peh-hue-juwa-chi-chhau" derived from *Mollugo* spp. and other comparative *Hedyotis* spp. will be reported in the next paper.

Experimental

Materials:

The samples were collected from the following stores:

1. Hu-lu-dun Chinese Herb Store (葫蘆墩中藥房), Fengyuan, Taichung Hsien, Dec. 25, 1983. (Identified as "Peh-hue-juwa-chi-chhau" A)
2. Ssu-chih Herb Store (四知青草店), Taipei, May 19, 1984. (Identified as "Peh-hue-juwa-chi-chhau" A)
3. Chi-tsao-tang Herb Store (吉草堂青草舖), Hsinchu, Feb. 3, 1985. (Identified as "Peh-hue-juwa-chi-chhau" A)
4. Fu-ben Herb Store (福本草藥鋪), Chiayi, May 3, 1984. (Identified as "Peh-hue-juwa-chi-chhau" A)
5. San-huo Herb Store (三和青草店), Kaohsiung, Aug. 13, 1984. (Identified as "Peh-hue-juwa-chi-chhau" A)

TABLE I. The Morphological Characteristics of the "Peh-hue-juwa-chi-chhau" *Hedyotis diffusa* WILLD., *H. corymbosa* LAM. and *H. tenelliflora* BLUME

Elements		Species		
		"Peh-hue-juwa-chi-chhau" A and *Hedyotis diffusa*	"Peh-hue-juwa-chi-chhau" B and *H. corymbosa*	"Peh-hue-juwa-chi-chhau" C and *H. tenelliflora*
External				
Leaf	form	linear or linear-lanceolate	linear-lanceolate	linear-lanceolate
	size (cm)	1–3 × 0.15–0.3	1–2.5 × 0.2–0.5	2–3 × 0.25–0.4
	apex	attenuate	narrowly acute	acute
	base	narrowed	narrowly acute	acute
Flower	type of flower	raceme	cymes	spike
Pedicel	length of pedicels (mm)	2–12	3–10	—
Peduncle	length of peduncles (mm)	—	5–12	—
Internal				
Leaf	length of needle crystals (μm)	35–65	20–50	55–75
	diameter of clustered crystals (μm)	10–25	7.5–10	10–15
	surface view: shape of upper epidermal cells	pentagonal, hexagonal-polygonal	irregular-polygonal	ovate, pentagonal, hexagonal-polygonal
	size of stomata (μm)	20–35 × 12.5–22.5	20–25 × 10–12.5	22.5–37.5 × 17.5–20
Stem	outline of cross-section	nearly circular	somewhat circular with 4-angled	nearly elliptical with 4-angled
	existence of papilla	+	—	—
	length of needle crystals (μm)	30–40	15–20	15–50
	diameter of clustered crystals (μm)	7.5–10	—	15–30
	existence of collenchyma of 4-angled	—	+	+
	existence of starch grains	—	—	+
Root	existence of clustered crystals (in cx)	—	—	+
	No. of medullary rays	indistinct	1–2	indistinct
	existance of starch grains	+	—	+

6. Han-chiang Herb Store (漢強百草店), Taichung, Feb. 3, 1985. (Identified as "Peh-hue-juwa-chi-chhau" A)
7. Fu-sheng Chinese Herb Store (福生中藥行), Hengchun, Pintung Hsien, Jan. 25, 1984. (Identified as "Peh-hue-juwa-chi-chhau" A)
8. Bai-he Herb Store (百荷青草店), Fangliao, Pintung Hsien, Oct. 3, 1983. (Identified as "Peh-hue-juwa-chi-chhau" A)
9. Lin Chinese Herb Store (林藥局), Kaohsiung, May 17, 1984. (Identified as "Peh-hue-juwa-chi-chhau" A)
10. Yong-feng Chinese Herb Store (永豐藥房), Nantou Hsien, Jul. 6, 1983. (Identified as "Peh-hue-juwa-chi-chhau" A)
11. Tian-yuan Chinese Store (天元中藥房), Hsikang, Taitung Hsien, Dec. 28, 1983. (Identified as "Peh-hue-juwa-chi-chhau" A)
12. Guang-hua Herb Store (光華草藥店), Kaohsiung, Jan. 25, 1984. (Identified as "Peh-hue-juwa-chi-chhau" B)
13. Hsin-fu-shan Herb Store (新富山草藥店), Chiayi, Dec. 28, 1983. (Identified as "Peh-hue-juwa-chi-chhau" B)
14. Chi-yuan-tang Herb Store (吉源堂青草舖), Changhua, Dec. 28, 1983. (Identified as "Peh-hue-juwa-chi-chhau" B)
15. Chun-ji Herb Store (春記草藥行), Hsinchu, Dec. 21, 1983. (Identified as "Peh-hue-juwa-chi-chhau" B)
16. Yu-ming-tang Herb Store (育明堂草藥房), Fengshan, Kaohsiung Hsien, Jan. 13, 1985. (Identified as "Pehhue-juwa-chi-chhau" B)
17. Yong-an Herb Store (永安青草店), Ilan, Jul. 24, 1985. (Identified as "Peh-hue-juwa-chi-chhau" B)
18. First market (第一市場), Taichung, Nov. 18, 1984. (Identified as "Peh-hue-juwa-chi-chhau" C)

Comparative plants

1. *Hedyotis diffusa* WILLD.
   Fangliao, Pingtung Hsien, Nov. 10, 1984.
   Lian-hua-chi, Nantou Hsien, Jun. 13, 1985.
   Yin-ho-ton, Taipei Hsien, May 8, 1983.
2. *Hedyotis corymbosa* LAM.
   Da-shu, Kaohsiung Hsien, Aug. 22, 1984.
   Fangliao, Pingtung Hsien, Nov. 10, 1984.
   Kao-shu, Pingtung Hsien, Apr. 20, 1983.
   Liokuei, Kaohsiung Hsien, Jul. 10, 1979.
3. *Hedyotis tenelliflora* BLUME.
   Keelung, Nov. 18, 1984.
   Sun-moon-lake, Nantou Hsien, Jun. 13, 1985.
   Yin-ho-ton, Taipei Hsien, May 8, 1983.

External morphology

The crude drugs are usually dried plants, but sometimes they are fresh plants.

1. "Peh-hue-juwa-chi-chhau" A and *H. diffusa* Fig. 1-A.

The drug occurs in dried entire plants or broken pieces, or in fresh state. The leaves are sessile, opposite, linear or linear-lanceolate, about 1 to 3 cm long and 1.5 to 3 mm wide, vinlets obscure, attenuate at the apex, and narrowed at the base. The margin is revolute with some fine serrulate hairs. The herb is branched, slender, glabrous, about 15 to 28 cm high and the stem is nearly rounded about 1 mm to 1.5 mm in diameter. The flowers are white, solitary or pairs in axillary racemes, and the pedicels are about 2 to 12 mm long. The roots attain a diameter of 1.5 to 5 mm.

The dried parts are brown to dark-green, while the fresh plants are green.

2. "Peh-hue-juwa-chi-chhau" B and *H. corymbosa* Fig. 3-A.

The general morphological characteristics of *H. corymbosa* are similar to those of *H. diffusa*, but differ in the following features:

The leaves are linear-lanceolate, about 1 to 2.5 cm long and 2 to 5 mm wide, narrowly acute at the apex and base. The herb are rarely scaberulous, about 10 to 40 cm high and the stems are definitely 4-angled. There are 1 to 4 flowers in axillary and terminal cymes with peduncles about 5 to 12 mm long and pedicels about 3 to 10 mm long.

3. "Peh-hue-juwa-chi-chhau" C and *H. tenelliflora* Fig. 5-A.

The general morphological characteristics of *H. tenelliflora* are similar to those of *H. diffusa*, but differ in the following features:

The leaves are about 2 to 3 cm long and 2.5 to 4 mm wide, acute at the apex and base. The herbs are about 19 to 45 cm high. The flowers are sessile, 1–5 clustered and in axillary spike. The roots are about 1 to 2 mm in diameter. The dried parts are blackish-brown.

Internal structures

1."Peh-hue-juwa-chi-chhau" A and *H. diffusa*

(Leaf) Fig. 1-B_{1-6}

A transverse section is obtained from 1/2–1/3 portion of a leaf for microscopic observation. The outline of transverse section is nearly circular. The cross-section through the midrib shows that the upper surface is slightly

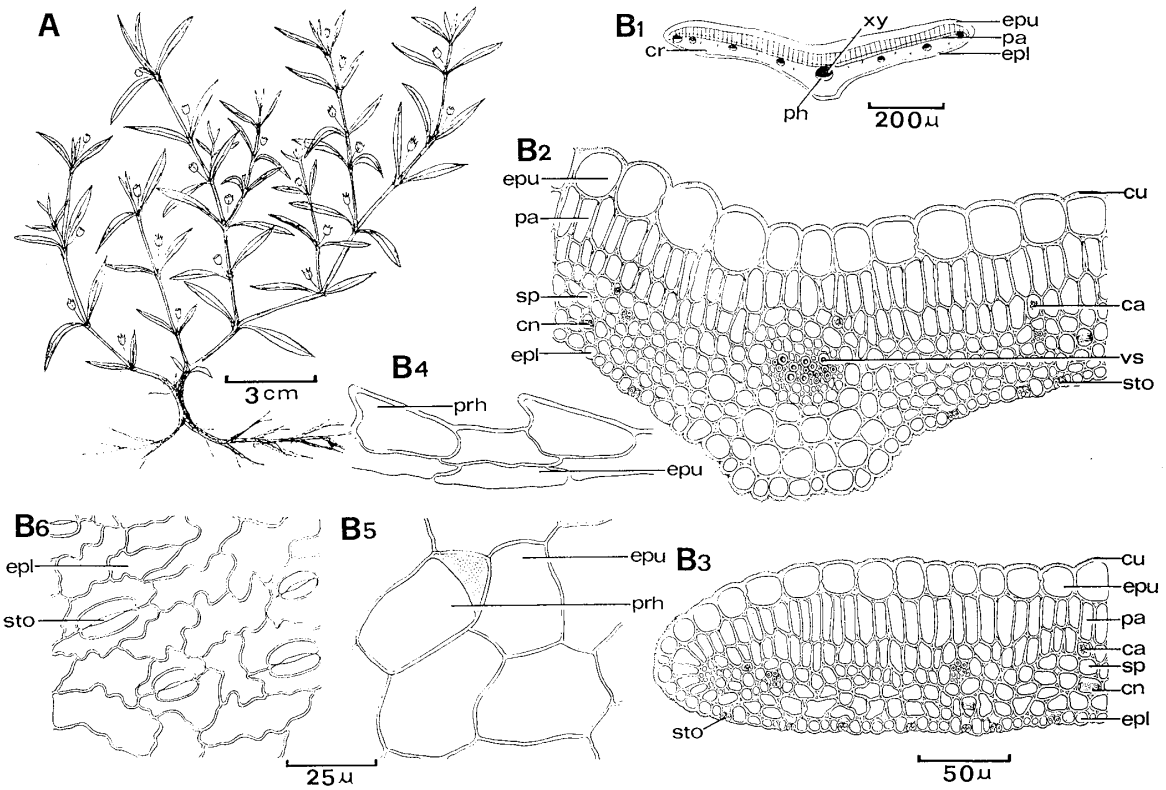

Fig. 1. "Peh-hue-juwa-chi-chhau" A and *Hedyotis diffusa*
A. sketch of the entire plant; B. transverse section of the leaf, 1 diagram; 2–3 detailed drawing of midrib and edge; 4–6 surface view of epidermis.

concave, and that the lower surface is distinctly convex. The upper epidermis of the midrib and the lamina consists of a layer of elliptical to oblong cells varying from 70 to 120 μm in long diameter and 60 to 100 μm in short diameter. The lower epidermis of that is composed of stomata and elliptical to ovate cells about 10 to 50 μm in long diameter and 10 to 25 μm in short diameter. Both upper and lower epidermises are covered with a smooth to denticulate cuticle. Sometimes can be found the thick wall epidermal cells near the margin.

The palisade tissue is composed of one to two layers of cylindrical or oblong cells varying from 40 to 70 μm in long diameter and 20 to 30 μm in short diameter, some cells as small as 25 to 35 μm in long diameter and 20 to 25 μm in short diameter. The spongy tissue consists of elliptical to polygonal cells measuring from 10 to 20 μm in diameter. Some cells in the mesophyll contain calcium oxalate in raphides about 35 to 65 μm in length and in clustered crystals about 10 to 25 μm in diameter. The vascular bundles of midrib and lateral veins are collateral. The xylem portion is composed of spiral vessels having a diameter of 5 to 12.5 μm and wood parenchyma cells about 10 to 15 μm in diameter.

Surface view of the upper epidermis reveals pentagonal or hexagonal to polygonal cells and prickle-hairs of non-glandular unicellular cell about 60 to 100 μm high; That of the lower epidermis exhibits irregular epidermal cells and elliptical stomata of Rubiaceous type, surrounded by 2 neighboring cells. The size of stomata is about 20 to 35 μm in long diameter and 12.5 to 22.5 μm in short diameter.

(Stem) Fig. 2-A_{1-2}

A transverse section is obtained at a 1/2 portion of an internode from a stem for microscopic observation. The cross-sections are nearly circular and show an outer cortical tissue and a central stele. The outermost tissue is epidermis composed of elliptical, rectangular to oblong cells about 15 to 35 μm in diameter and 10 to 15 μm in short diameter, and covered with a denticulate cuticle. The papillae about 20 to 35 μm in length and stomata in very small number can be found on the epidermis. Beneath the epidermis, the cortex consists of 3 to 4 layers of thin-walled, circular, elliptical to oblong parenchyma cells varying from 15 to 25 μm in long diameter and 15 to 20 μm in short diameter. The collateral vascular bundles are arranged to form a ring just inner to the cortex. The xylem contains vessels, tracheids, wood parenchyma and wood fibers. The vessels are about 20 to 40 μm in diameter, having simple perforations, with pitted and reticulate thickenings, whose length measure from 225 to 490 μm, and 175 to 257.5 μm respectively. The tracheids have spiral, pitted and scalariform thickings and the diameter of that are about 15 to 20 μm. The length of pitted trachieds varies from 100 to 122.5 μm and that of scalariform tracheids about 150 to 200 μm, some down to 95 μm. The wood parenchyma cells have a diameter of 15 to 30 μm. The wood fibers are about 310 to 710 μm in length and 5 to 15 μm in diameter. The pith, comprising the widest part of

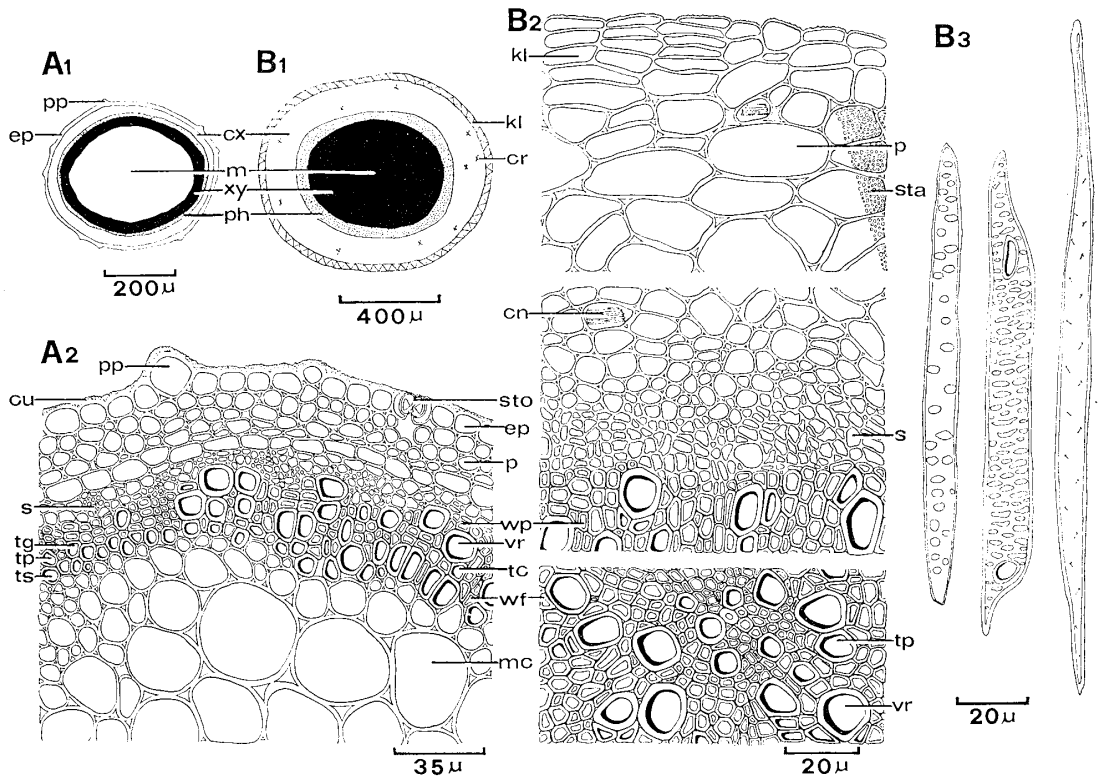

Fig. 2. "Peh-hue-juwa-chi-chhau" A and *Hedyotis diffusa*
A. transverse sections of the stem. 1. diagram; 2. detailed drawing. B. transverse sections of the root. 1. diagram; 2. detailed drawing. 3. elements of the xylem of maceration.

the stem, is made up of elliptical to ovate parenchyma cells about 35 to 85 μm in long diameter and 30 to 75 μm in short diameter. Scattered within the cortex and pith are several cells containing calcium oxalate in raphides about 30 to 40 μm in length, and clustered crystals about 7.5 to 10 μm in diameter.

(Root) Fig. 2-B_{1-2-3}

A transverse section is obtained at a distance of about 2 cm from the proximal end. The cross-sections appear more or less circular-shaped in outline and reveal an outer cortical portion and a central stele. The outermost tissue is cork layer consisting of 3 to 5 layers or rectangular to oblong cells about 15 to 55 μm in long diameter and 10 to 15 μm in short diameter. Beneath cork layer, the cortex is composed of several layers of thin-walled, circular, elliptical or enlongated oblong parenchyma cells, having 27.5 to 70 μm in long diameter and 17.5 to 65 μm in short diameter. Some cells in the cortex contain calcium oxalate in raphides about 45 to 55 μm in length.

The vascular bundles are collateral. Central part of the root is occupied by a core of xylem, with indistinct medullary rays. The xylem portion consists of vessels, tracheids, wood parenchyma and wood fibers. The vessels are with reticulate thickenings, measuring from 20 to 35 μm in diameter, 155 to 250 μm in length, some as small as 82.5 to 120 μm and have simple perforations. The pitted tracheids vary 10 to 20 μm in diameter and 135 to 217.5 μm in length, some as small as 27.5 to 97.5 μm. The wood fibers have a diameter of 100 to 355 μm.

2. "Peh-hue-juwa-chi-chhau" B and *H. corymbosa*

The general structures are similar to those of *H. diffusa* but differ in the following features:

(Leaf) Fig. 3-B_{1-6}

The upper epidermis of the midrib and the lamina consists of a layer of rectangular, elliptical to irregular cells varying from 25 to 115 μm in long diameter and 30 to 70 μm in short diameter. The size of lower epidermal cells are about 15 to 40 μm in long diameter and 20 to 35 μm in short diameter. The palisade cells measure from 12.5 to 55 μm in long diameter and 10 to 15 μm in short diameter. In the mesophyll can be found calcium oxalate in raphides and clustered crystals, the former measure from 7.5 to 10 μm in diameter and the latter has the length varying from 20 to 50 μm. The diameter of the spiral vessels are about 7.5 to 12.5 μm and that of the wood parenchyma cells about 5 to 15 μm. Surface view of the upper epidermis reveals irregular to polygonal cells. The size of stomata is about 20 to 25 μm in long diameter and 10 to 12.5 μm in short diameter.

(Stem) Fig. 4-B_{1-2}

The cross-sections are somewhat circular with four distinct angles. In the angles, there are 4 well-defined groups of collenchyma, consisting of 3 to 5 layers of elliptical to polygonal cells, varying from 15 to 25 μm in long diameter and 10 to 20 μm in short diameter. Calcium oxalate in raphides can be found in the cortex and pith, having a length

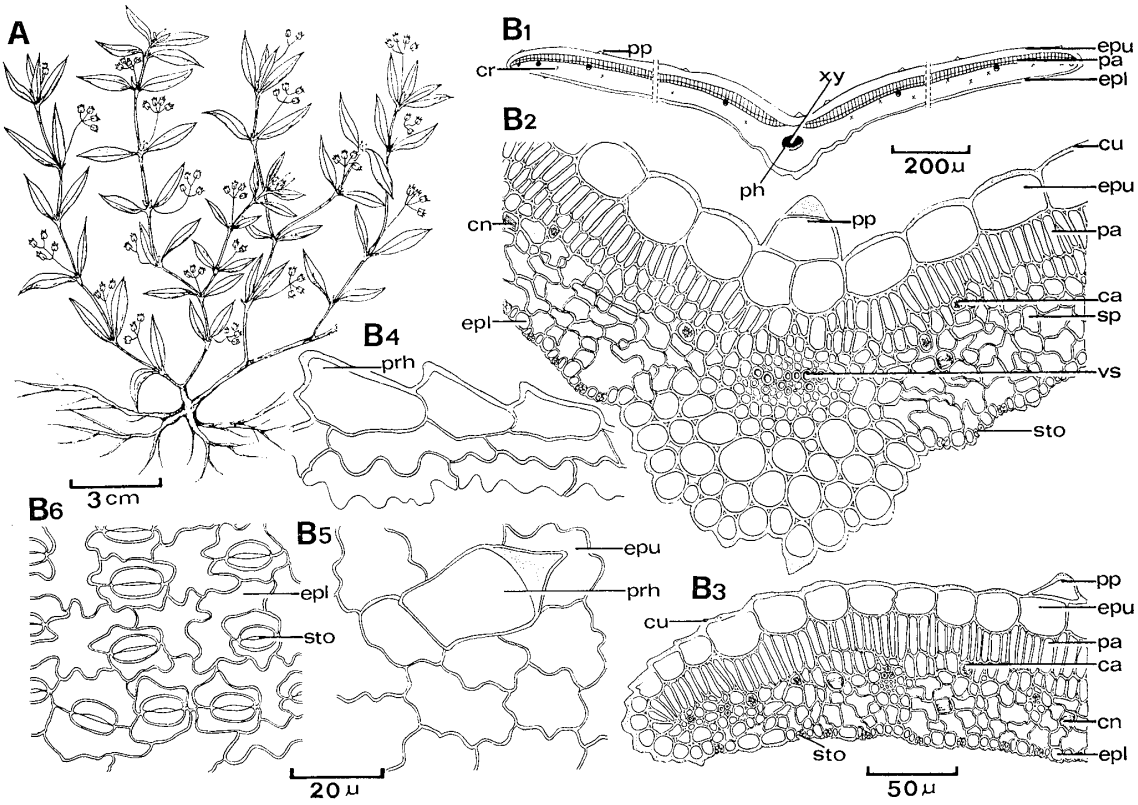

Fig. 3. "Peh-hue-juwa-chi-chhau" B and *Hedyotis corymbosa*
A. sketch of the entire plant; B. transverse section of the leaf, 1 diagram; 2–3 detailed drawing of midrib and edge; 4–6 surface view of epidermis.

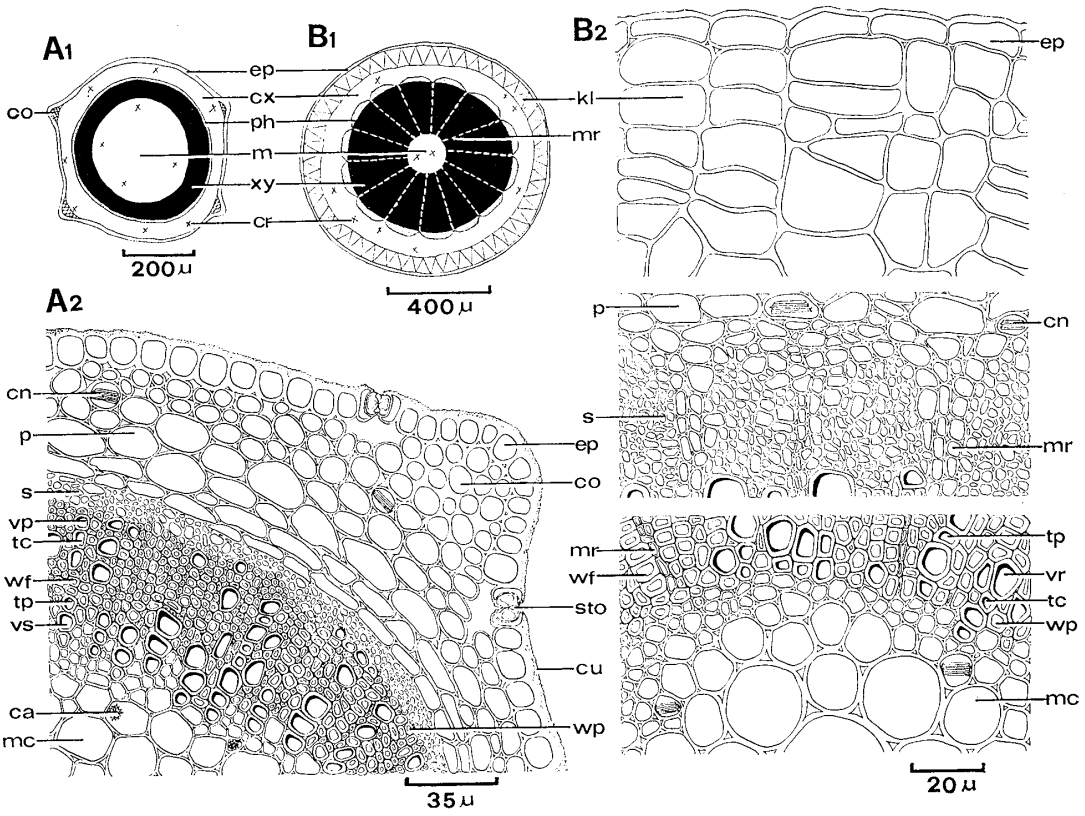

Fig. 4. "Peh-hue-juwa-chi-chhau" B and *Hedyotis corymbosa*
A. transverse sections of the stem. 1. diagram; 2. detailed drawing. B. transverse sections of the root. 1. diagram; 2. detailed drawing.

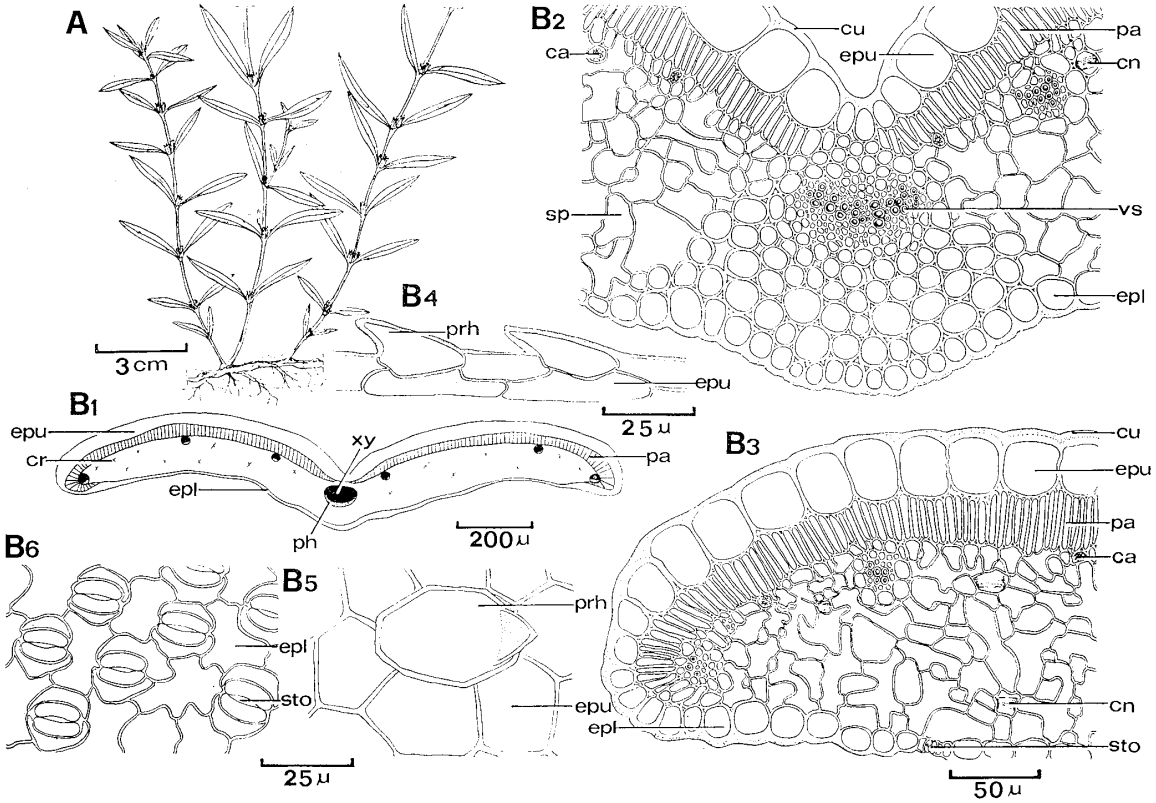

Fig. 5. "Peh-hue-juwa-chi-chhau" C and *Hedyotis tenelliflora*
A. sketch of the entire plant; B. transverse section of the leaf, 1 diagram; 2–3 detailed drawing of midrib and edge; 4–6 surface view of epidermis.

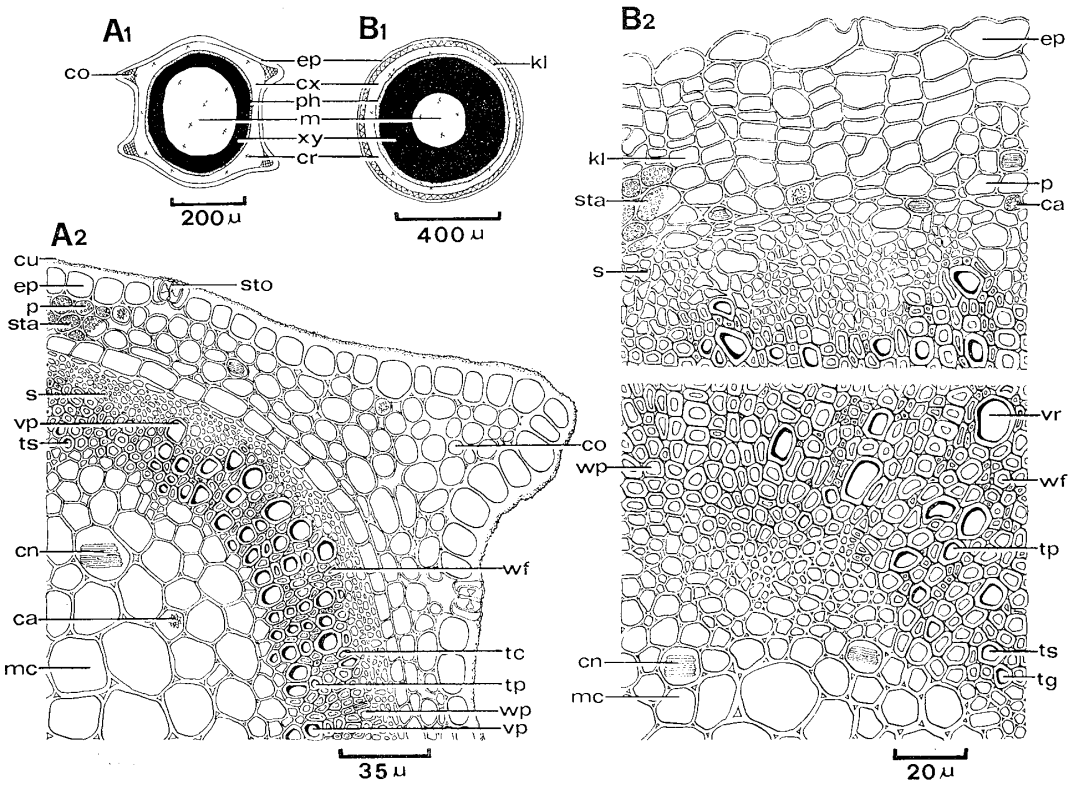

Fig. 6. "Peh-hue-juwa-chi-chhau" C and *Hedyotis tenelliflora*
A. transverse sections of the stem. 1. diagram; 2. detailed drawing. B. transverse sections of the root. 1. diagram; 2. detailed drawing.

of 15 to 20 μm.

(Root) Fig. 4-B_{1-2}

The outermost layer is epidermis which consists of a layer of elliptical, rectangular or oblong cells measuring from 15 to 50 μm in long diameter and 10 to 20 μm in short diameter, but easily falls off.

The medulla consists of thin-walled, circular, elliptical or hexangular cells, having 7.5 to 50 μm in long diameter and 5 to 30 μm in short diameter. The medullary rays are distinct, composed of 1 to 2 series upright of ovate-oblong cells, varying from 10 to 25 μm in long diameter and 5 to 10 μm in short diameter.

3. "Peh-hue-juwa-chi-chhau" C and *H. tenelliflora*

The general structures are similar to those of *H. diffusa*, but differ in the following features:

(Leaf) Fig. 5-B_{1-6}

The cross-section through the midrib shows that upper surface is distinctly concave. The palisade tissue consists of a layer of cylindrical cells having 40 to 60 μm in long diameter and 10 to 15 μm in short diameter. The spongy cells are polygonal or irregular and arranged loosely. Some cells in the mesophyll contain calcium oxalate in raphides about 55 to 75 μm and in clustered crystals about 10 to 15 μm in diameter.

(Stem) Fig. 6-A_{1-2}

The outline of transverse sections are nearly elliptical with four distinct angles. In the angles, there are 4 well-defined groups of collenchyma, consisting of 4 to 6 layers of circular to elliptical cells measuring from 15 to 35 μm in long diameter and 20 to 30 μm in short diameter. Scattered within the cortex and pith are several cells containing calcium oxalate in raphides about 15 to 50 μm in length, and clustered crystals about 15 to 30 μm in diameter. Starch grains also can be found in the cortex and pith, globular, single, about 2.5 to 5 μm in diameter.

(Root) Fig. 6-B_{1-2}

The outermost layer is epidermis which consists of a layer of ovate, elliptical or irregular cells varying from 30 to 60 μm in long diameter, and 25 to 50 μm in short diameter, but easily falls off. Calcium oxalate in clustered crystals can be found in medulla, measuring from 10 to 15 μm in diameter. The medulla is composed of elliptical cells varying from 35 to 75 μm in long diameter and 30 to 70 μm in short diameter and medullary rays are indistinct.

Results and Discussion

1. The characteristics of external and internal structures of "Peh-hue-juwa-chi-chhau", *Hedyotis diffusa* WILLD., *H. corymbosa* LAM. and *H. tenelliflora* BLUME are shown in Table I. From the observations of leaf (form, size, base, apex, thickness of midrib, length of needle crystals, diameter of clustered crystals, shape of upper epidermal cells, size of stomata), stem (outline of cross-section, existence of papilla, length of needle crystals, diameter of clustered crystals, existence of collenchyma of 4-angles, existence of starch grains), and root (existence of clustered crystals in cortex. No. of medullary rays, existence of starch grains), it is possible to identify the species of these three plants. The results show that "Peh-hue-juwa-chi-chhau", as found on Taiwan market is derived from the entire plants of the following plants: (A) *Hedyotis diffusa* WILLD. (B) *H. corymbosa* LAM. and (C) *H. tenelliflora* BLUME.

2. "Peh-hue-juwa-chi-chhau" is said to have anticancer, antitoxic, antipyretic and diuretic properties, in the treatment of cancers, appendicitis, enteritis, hepatitis, eye diseases, contusions, furunculosis, bleeding *etc.* Besides its formal name, "Peh-hue-juwa-chi-chhau" has several other names such as "Juwa-chi-chhau" (蛇舌草), "Long-tu-zhu" (龍吐珠), "Juwa-chi-huang" (蛇舌癀) "Zhu-zi-chhau" (珠子草), "Ding-jing-chhau" (定經草), and easily confused with other drugs which used the same name.

"Peh-hue-juwa-chi-chhau" have been also used in China mainland as a folk remedy for cancer, appendicitis, hepatitis, bronchitis, tonsillitis, pharyngitis, contusions, furunculosis, and snake bite etc. Their medical effects are very similar as in Taiwan.

3. In general, commercial drug "Peh-hue-juwa-chi-chhau" derived from *H. diffusa* WILLD. and *H. tenelliflora* BLUME can be found in the north and central part of Taiwan, whilst *H. diffusa* WILLD. and *H. corymbosa* LAM. in the south and central part of Taiwan.

It is reported that *H. diffusa* WILLD.[6] had anticancer property, and some of the anticancer components isolated from *H. diffusa* WILLD. were 2-methyl-3-hydroxy-anthraquinone, 2-methyl-3-methoxy-anthraquinone, 2-methyl-3-hydroxy-4-methoxy-anthraquinone.[7]

But *H. diffusa* WILLD., *H. corymbosa* LAM. and *H. tenelliflora* BLUME are used confusedly on Taiwan market, due to their external morphology being much similar to one another. It would be interesting that whether they have the same medical effect or not.

Abbreviations: **ca**: clustered crystal, **co**: collenchyma, **cn**: needle crystal, **cr**: crystal, **cu**: cuticle, **cx**:

cortex, **ep**: epidermis, **epl**: lower epidermis, **epu**: upper epidermis, **k**: cork cell, **kl**: cork layer, **m**: medulla, pith, **mc**: medullary cell, **mr**: medullary ray, **p**: parenchyma cell, **pa**: palisade parenchyma (tissue), **ph**: phloem, **pp**: papilla, **prh**: prickle hair, **s**: sieve tube, **sp**: spongy parenchyma (tissue), **sta**: starch grain, **sto**: stomata, **tc**: scalariform tracheid, **tg**: ring tracheid, **ts**: spiral tracheid, **tp**: pitted tracheid, **vp**: pitted vessel, **vr**: reticulate vessel, **wf**: wood fiber, **wp**: wood parenchyma, **xy**: xylem

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