

## "PODOPHYLLUM EMODI."

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Podophyllum is a small herbaceous plant belonging to the family *Berberidaceæ*. There are in all four species of this plant known. *P. peltatum* grows in North America. It is this species which is at present the chief source of the popular purgative podophyllin. *P. emodi* (Wall) grows in Northern India and also in Tibet and Afghanistan. This species has, comparatively speaking, only recently attracted the notice of the scientific world and its claims to be included in the British Pharmacopœia are now being considered. The other two species, namely, *P. pleianthum* (Hance) and *P. versipelle* (Hance), are met with in China. They are only of botanical interest. The Reporter on Economic Products first noticed this plant in Kulu, during a botanical trip there in November 1888. It was afterwards found in Garhwal, Kumaun, Chamba and the hills near Simla, Kashmir and Hazara. It is also met with in Sikkim, Tibet and Afghanistan. The plant grows less plentifully in the eastern part of the Himalayas than in the western and central parts of the range. It does not occur below an altitude of 6,000 feet and generally is only found at an elevation of 8,000 to 9,000 feet though sometimes up to 15,000 feet. Though the plant is met with in Garhwal, and north-west of Simla in the Shalai and other hills, it is most abundant in the western hills of Simla and in Kumaun, in Chamba and Kulu where the hill slopes are often practically covered with it.

## DESCRIPTION AND HABITS.

As mentioned above, it is a herbaceous plant rarely attaining a greater height than one foot. The root system is perennial and it consists of one rhizome with numerous thin rootlets branching off from it. Above it is the succulent stem growing annually and bearing from one to five leaves according to the age of the plant. The plants generally appear in April and die down in November. The leaves usually appear when the stem has attained a height of 6" to 12", and hang umbrella-like on either side of it. It flowers in May and the flower is white with a pinkish tinge. The fruit ripens about August and September. It is of the size and shape of a small lemon. Attempts are being made to cultivate this plant and it has been observed that it can be grown from sections of the rhizome as well as from seed, but the former method generally takes a longer time than the latter. It grows two years after planting the sections but it is only after the fourth and fifth year that the rhizome is fit for collection.

## ITS MEDICINAL PROPERTIES.

As in the American species the active principle is found only in the rhizome and rootlets branching off from it. The resin extracted from the rhizome is an hydragogue cathartic in large doses and an alterative in small. The activity of the resin depends on the chief active principle called *podophyllotoxin*. From its vernacular name *papra* or *papri*, also *bhavan bakra* or *bakara* which are given in the new *Pharmacographia Indica*, it is supposed that it was one of the bile expelling plants known to Sanskrit writers under the name *Papрати*. In Chamba and Kulu they are known as *Gulkakri* or *Bhavan kark* respectively. The similarity in names shows that the same property is attributed to it. In some places indeed it is used as a jalap. It is known to have a specific action on the liver causing an increased secretion from the bile. But unlike jalap, if taken by itself it causes severe griping and pain and is thus rarely used. In some cases it serves the same purpose as calomel.

## ITS CONSTITUENTS AS COMPARED WITH THE AMERICAN SPECIES.

The Reporter on Economic Products, when he first noticed this plant in 1888, at once thought of having it chemically examined to determine if in its constituents and their medicinal properties it would compare favourably with the American species. Accordingly, he sent some roots to Dr. Dymock of Bombay for chemical examination who, in conjunction with Mr. Hooper, instituted a comparative examination of the two species and reported that the Indian species contains more than twice as much podophyllum resin as the American. According to Mr. Hooper *P. emodi* contains 12 per cent of the resin whereas the other contains only 4 per cent, and both are similar in their physiological activity. In 1898 Professor Dunstan, together with Dr. Henry, made a complete investigation into the chemistry of both the species. *P. peltatum* had already been examined by many chemists, but it was Podwysotski (Pharm. Journal, iii, 7, 12, 217, 1011) who made the first important contribution on the subject.\* He proved that the resin did not contain any alkaloid such as berberine. He obtained three substances *Podophyllotoxin*, *Podophyllic acid* and *Podophylloquercetin*. He also showed that when *podophyllotoxin* is acted on by alkalies, it is converted into two new substances *Picropodophyllin* and *Picropodophyllic acid*, the former of which is crystalline and the latter gelatinous. Kursten amplified on this work and obtained *podophyllotoxin* in a crystalline form and believed that along with the isomeric *picropodophyllin* formed by the action of alkalies on *podophyllotoxin*, an oxidation product is formed which is gelatinous and is identical with Podowysotski's *picro-podophyllic acid*.

Dunstan and Henry give the following constituents of *P. emodi* and prove that *P. peltatum* is identical with it in composition. According to them the crystalline *podophyllotoxin* has the composition  $C_{18}H_{14}O_6 \cdot 2H_2O$ . When acted on by aqueous alkalies it is converted into its isomeric compound *picro-podophyllin*. It was also shown that both the above-mentioned isomers contained two methoxyl groups. They also isolated the podophyllic acid to

\* See Imperia' Institute Technical Reports and Scientific Papers, 1903.

which they assigned the formula  $C_{15} H_{10} O_7$ . The yellow colouring matter was also carefully separated and purified. It was shown to have the formula  $C_{15} H_{10} O_7$  and to yield a pentacetyl derivative melting at  $192^{\circ}C$ . This substance is identical with *quercetin*. But even after *picropodophyllin* and *podophylloquercetin* has been removed a dark brown resin is left behind. It is amorphous and completely soluble in alcohol. This was also shown to be physiologically active though not so irritating as *podophyllotoxin* which cannot by itself be used as a medicine. To sum up *Podophyllum emodi* like *Podophyllum peltatum* contains the following substances:— (1) *Podophyllotoxin*, (2) *Podophyllic acid*, (3) *Podophylloquercetin* and (4) *Podophyllum resin*. *Picropodophyllin* is not a constituent of the herb but can be prepared from *podophyllotoxin* and is an isomer of it.

COMPARATIVE ESTIMATION OF PODOPHYLLUM RESIN AND  
PODOPHYLLOTOXIN IN TWO SPECIES.

Hooper and Dymock were the first to make a comparative estimation of the amount of resin in the two species. According to them the percentage was about 11 per cent in the Indian species and 4 to 5 per cent in the American one. Umney found the percentage to be 12 per cent in *Podophyllum emodi*. Dunstan and Henry found 9—12 per cent of resin in the Indian root and 4—5 per cent in the American. They also showed that the Indian drug contains 2—5 per cent of *Podophyllotoxin* while the American contains only .8 to .9 per cent. In regard to the variation in the resin per cent of the Indian roots, it may be mentioned that the writer had the opportunity to examine samples of *P. emodi* roots from different localities collected in the different seasons and he has shown (see Forest Bulletin No. 9) that the percentage of resin in the Indian roots varies from 10 to 20 and that of the toxin in the resin from 25 to 50 according to the locality and the season of collection, and it is safe to assert that an average sample of the Indian root will contain, as a rule, twice as much of the active principle as the American. It has also been determined that the best season for collection is May, when the herb is in flower. In

order to obtain the Indian drug of standard and regular composition, it is essential that it should be cultivated and collected under similar conditions in a systematic manner. It is gratifying to note that the Forest Department is looking into the experimental cultivation of this valuable drug.

Doctors Mackenzie and Dixon of St. Thomas Hospital have made a comparative investigation of the medicinal properties of these two herbs and proved that the resin from *P. emodi* is as good a purgative agent as that obtained from *P. peltatum* when administered in small quantities but acts more powerfully when given in large doses. The chief physiological and therapeutical properties of the various constituents of the herbs can very well be understood from the following statement of the authors :—

“That Indian Podophyllin is an active purgative and a useful therapeutic agent; that it may be substituted for *P. peltatum*. But it is important that the physician should know which sample he is prescribing, as the Indian variety is nearly twice as physiologically effective as the American. That the active principles contained in the crude resin are two substances—(a) Crystalline *podophyllotoxin*; (b) *podophyllo-resin*,—both of which act as excellent laxatives in small doses, without secondary constipation or other objectionable symptoms.”

“That although both these substances act very similarly on the alimentary tract, it is only the podophyllo-resin which exerts a true cholagogue effect, which shows itself rather by a large increase of the solids secreted than by an increased quantity.”

“Both exert their specific activity when injected hypodermically in alcoholic solution, but in man so much irritation is produced as to forbid their employment in this manner.”

It has been shown that the rhizome of *P. emodi* of India is twice as active as that of the American *P. peltatum*. They are identical in their chemical composition and in their physiological

and therapeutic properties. All scientific authorities are unanimous in their preference of *P. emodi* as a medicine to *P. peltatum*, though exception is taken in certain quarters as to the constancy of its composition. It has been pointed out that this difficulty can be overcome by artificial cultivation of the rhizome under uniform conditions.

It has been included in the Addenda of the British Pharmacopœia, but it has not yet got its due place in the B. P. official list, and because of this want of full recognition, it does not fetch at present a remunerative price. For example, a Calcutta exporter obtained only 34 shillings per cwt. c. i. f. London for rhizome containing 13 per cent of this resin. This rate is extremely low considering the superior quality of *Podophyllum emodi*. At this rate, it is hardly worth while to cultivate it or even to collect it. It may not be therefore out of place to draw the attention of the Committee appointed for the revision of the British Pharmacopœia to the claims of *Podophyllum emodi* for inclusion in the revised edition.

The price of the Podophyllin or the Podophyllum resin obtained from the American plant is about 9 shillings per lb. in London. The Indian rhizome contains about 11 per cent, and 1 cwt. of it would give about 12 lbs. of the resin worth 108 shillings. Once it becomes fully recognised by the B. P., it will be worth while to manufacture the Podophyllum resin in India and thus realise its full value instead of exporting the rhizome at 38 shillings per cwt. as at present.

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