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Botanical Medicine Monographs and Sundry

THE DISTRIBUTION OF SAFROL.

By PROFESSOR FLÜCKIGER.

The prevailing constituent of the essential oil of sassafras root is Safrol, as will be seen in the text-books; for instance, in 'Pharmacographia,' second edition p. 536. In the crude oil, safrol is held in solution by the hydrocarbon safrene, C₁₀H₁₆, and may be separated either by fractional distillation or by cooling the oil. Safrol liquefies at 12º (53.6°F.) and yields very large and fine prisms, which I caused to be exactly investigated crystallographically by Professor Arzcuni, as mentioned in 'Pharmacographia.' The large crystals of safrol are very little softer than those of gypsum. Although they cannot be kept at a temperature exceeding their melting point, they were, curiously enough known in England a century and a half ago.

As to the constitution of safrol it has been shown by Eykman that by means of permanganate of potassium it yields piperonylic acid

\[ C₆H₃(O>CH₂)COOH, \]

safrol, therefore, may be represented by the formula—

\[ C₆H₃(O>CH₂)CH₂:\]

\[ \text{CH}_3 \]

Piperonylic acid is obtained by oxidizing piperonal (now known, in perfumery, under the name of heliotropin)—

\[ C₆H₃(O>CH₂)CHO \]

and Poleck thinks that he has observed piperonal among the products of the treatment of safrol with permanganate of potassium, for the action of this salt on safrol is by no means very simple, 4 per cent. of piperonylic acid only having been obtained by Poleck.

Sassafras is not the only plant containing safrol. In the same natural order viz. that of Lauraceae, Mespilodaphne Sassafras, Meissner, a Brazilian tree, has a bark resembling safrol in odor. The same is also well known with regard to the Puchury nuts, or sassafras nuts, the cotyledons of two Brazilian species of Nectandra, a genus
as yet very imperfectly known.

Again, the order of Monimiaceae, tribe Atherospermeae, closely allied to Lauraceae, would appear to be provided with safrol. Of this at least the aroma of the Australian 'sassafras bark' is strongly suggestive. This drug, which is not seldom seen in the London market, is the bark of Atherosperma moschatum, Labillardiére, a tree indigenous to Australia and Tasmania. The bark of Doryphora Sassafras of New Caledonia, likewise of the order of Monimiacea—Atherospermeae, also smells of sassafras.

Although there can be but little doubt as to safrol really occurring in all those essential oils of the just-named plants the fact has not yet been proved.

This, however, has been most surprisingly done by the well-known house of Schimmel & Co., of Leipzig, with regard to the oil of the camphor tree Cinnamomum Camphora. Since 1885 the said house is manufacturing safrol from camphor oil to a very large extent. No doubt there is now much more safrol being made in the state of absolute purity at Leipzig than they are able to distil crude oil of sassafras in the United States.

Cinnamomum Parthenoxylon, Meissner, and C. glanduliferum, Meissner, the former tree belonging to the forests of Penang, Sumatra and Java (Kayu-gadis of the Malays), perhaps also in Tennasserim; the second in Nepal, Sikkim, Bhootan and Khasia ("Sassafras of Nepal"), are also known for their odor resembling that of true sassafras. They would deserve a chemical investigation.

I am struck, lastly, with the very strong odor of the same kind displayed by the bark of an Australian tree, which has been described by Bentham (assisted by Ferdinand Müller) in the 'Flora Australiensis,' vol. v. (1870), p. 299, under the name of Nesodaphne obtusifolia. It is a large and handsome tree, growing in Queensland, Rockingham Bay, Fitzroy River, Rockhampton, Archer's Creek (according to Leichhardt), also in New South Wales, Clarence River. Hooker and Bentham, 'Genera Plantarum,' iii. (1880), p. 152, ultimately unite the genus Nesodaphne to Beilschmiedia; the tree under notice is, therefore, to be called Beilschmiedia obtusifolia, Benth. and Hook.

Dr. Joseph Bancroft, in his 'Contributions to Pharmacy from Queensland' (Colonial and Indian Exhibition of 1886, London), p. 11, states that the tree grows in the rich scrubs to the north of Brisbane. Its grey, rough bark, reddish-brown internally, has a strong aromatic odor and pleasant astringent taste, and is frequently used by bushmen to improve the flavor of their tea. The bark, according to Mr. Staiger, affords about 2 per cent. of volatile oil heavier than water, and 9 per cent. of tannin.

Being indebted to Mr. E. Merck of Darmstadt, for a good sample of the bark of Beilschmiedia obtusifolia, I may state that it agrees to some degree, in its microscopic structure both with the bark of cassia lignea and sassafras. The Beilschmiedia bark is as much as 15 millimetres (half an inch) in thickness, and shows the same exfoliation due to secondary cork bands (rhytidoma) as the bark of sassafras. Beilschmiedia bark is, on the other hand, much more fibrous than either of
the above-named barks; its tissue being very rich in long thin fibres, and in its outer layer there are scattered, not in large number, sclerenchymatous cells, having comparatively thin walls. The oil ducts of Beilschmiedia bark are neither very numerous, nor considerably large. It remains to be proved that they really contain safrol as I venture to say.

In the natural system, the Magnoliaceae are not much distant from both Lauraceae and Monimiaceae. Eykman has shown that safrol also occurs in the essential oil of the fruit of *Illicium religiosum*, the false star-anise of Japan; this tree belongs to the order of Magnoliaceae. There the safrol is accompanied by eugenol, the formula of which

\[
\text{C}_6\text{H}_5 \text{OCH}_3 \quad \text{OH}
\]

at once reveals its relationship to safrol as also to anethol

\[
\text{C}_6\text{H}_4 \text{OCH}_3 \quad \text{CH}=\text{CH}--\text{CH}_3
\]

It would appear, therefore that at least eugenol \(\text{C}_{10}\text{H}_{12}\text{O}_2\) and safrol \(\text{C}_{10}\text{H}_{10}\text{O}_2\) may be in some generic relation. The former has been met with by Stenhouse in the leaves of the cinnamon tree. And, thirdly, anethol \(\text{C}_{10}\text{H}_{12}\text{O}\), the chief constituent of the oil of true star-anise, *Illicium anisatum*, is there replacing safrol as occurring in the other variety.

It would be interesting to be able to convert one into the other of those three highly aromatic substances; their empirical formulae: \(\text{C}_{10}\text{H}_{12}\text{O}\), \(\text{C}_{10}\text{H}_{10}\text{O}_2\), \(\text{C}_{10}\text{H}_{12}\text{O}_2\), would apparently indicate the probability of such transformations, but not their structure—Phar Jour. and Trans. June 4th, 1887) p. 989.

**INVESTIGATIONS ON STROPHANTHUS.**

From a paper by Mr. Wm. Elborne, published in Phar. Jour. and Trans., March 12, 1887, p. 743, we make the following extracts:

Strophanthus was introduced by Prof. Fraser, his researches having reference to the seeds of the Kombé arrow poison (See AMER. JOUR. PHAR., 1886, p. 405). From these seeds Fraser isolated a crystalline bitter glucoside, which he named strophanthin. From *Strophanthus hispidus*, De Cand., Hardy and Gallois subsequently isolated a crystalline bitter principle, neither of a glucosidal nor alkaloidal nature, but possessing all the toxic properties of Fraser’s glucoside, which they termed strophantine (AMER. JOUR. PHAR., 1877, p. 402). The botany of the subject is by no means at present sufficiently clear to enable pharmacists to distinguish with precision the one from the other, and it appears to be questionable whether poisonous seeds, possessing undoubtedly the physiological activity described by Fraser, may be here and are not collected from species other than the two already experimented upon by the above gentlemen. Prof. Oliver has stated that the fruits
entirely correspond in the two species; it is, however, generally accepted that the follicles yielding seeds with greenishbrown hairs, belong to the Kombé plant, whereas those yielding seeds with brown hairs, belong to the S. hispidus, and Prof. Oliver, after a more minute examination, referred the former to a distinct species which he named Strophanthus Kombé. This plant is described as follows by Dr. Kirk, Consul at Zanzibar:

“The plant is a woody climber, growing in the forest both of the valley and the hills, and found at various places between the coast and the centre of the continent above the Victoria Falls and the Zambesi. The stem is several inches in diameter and rough outside. The plant climbs up the highest trees and hangs from one tree to another like a bush-vine. The flowers are of a pale yellow, and last for but a short time during the months preceding the first rains of the season. (Oct and Nov).”

The fruit is ripe in June. the natives separate the rough epicarp, and mesocarp, and dry the endocarp containing the seeds; hence the tawny appearance of the commercial follicles.

The method adopted by the natives in poisoning their arrows, is as follows: Before extracting the seed from the fruits, they dig a hole in the ground, so that they can bury the comose hair attached to the seed (for fear of its flying in their eyes), they then coarsely grind the seed, and mix it into a paste, which latter constitutes the poison with which the arrows are smeared. Game wounded by an arrow thus poisoned
dies at once, seldom being able to move a hundred yards. The flesh is eaten without 
any evil effect accruing. The only precaution is to squeeze the sap out of a branch of 
the baobab tree into the wound made by the arrow, which is said to mitigate any evil 
effect that might result from the poison being more plentiful in the vicinity of the 
wound.

The drug examined by Mr. Elborne had been presented by Mr. T. Christy, and was 
collected in East Africa. Mr. E. M. Holmes found it to correspond with that from Lake 
Nyanza, which is referred to Str. Kombé. The seeds of Str. hispidus are chestnut-
brown. The hairs on the seed are quite deciduous, and the comose appendages are 
white. One of the pods, 12 inches in length, weighed 14.069 gm., and yielded seeds 5.99 
gm. (42 per cent.); comose hair 3.119 gm. (22 per cent.), and endocarp 4.96 gm. (35 
percent.)

On submitting the seeds to analysis, petroleum ether dissolved 20.8 per cent. of a 
bright yellow oil, having a tinge of green, free from bitter taste, and in a few days 
depositing some colorless crystals which were fusible, and on ignition left no ash. 
Absolute ether took up 0.9 per cent. of chlorophyll and fat, and the extract was free 
from bitterness. The absolute alcohol extract, after treatment with charcoal, was 
obtained in transparent scales weighing 1.5 per cent.; it was soluble in water, 
impacted bitterness to 380.000 of water, did not react with alkaloid reagents, was not 
precipitated by lead acetate, and did not reduce Fehling's solution until it had been 
boiled with dilute sulphuric acid. Cold distilled water extracted 22.5 per cent. of 
extract, which when dissolved in little water and poured into a large quantity of a 
mixture of alcohol and ether, precipitated albuminous matters, and by evaporation of 
the filtrate yielded an additional quantity of 2.9 per cent. of bitter principle, identical 
with the preceding in appearance, behavior and physiological action. The matter not 
dissolved by the foregoing treatment weighed 54.3 per cent. According to L. Larmuth, 
the bitter principle on being dissolved in water will, in a few days, undergo some 
change, and become far more toxic than when recently prepared.

The comose hairs yielded to absolute alcohol 0.68 per cent. of brown extract, from 
which water dissolved a very small amount of slightly bitter matter, not acted upon 
by alkaloidal reagents. The resinous residue was insoluble in ether; its alcoholic 
solution had a bitter taste, and dropped into water produced a beautiful blue 
fluorescence. The aqueous extract of the hairs was free from bitterness.

The endocarp gave with absolute alcohol 1.3 per cent. of extract, yielding with water a 
slightly bitter solution, free from tannin and not precipitated by Mayer's solution.

The root, freed from the cortical portion, excited sneezing when powdered, and yielded 
to ether 0.7 per cent. of caoutchouc-like substance; to alcohol 1.1 per cent. of an 
intensely bitter substance giving the reaction for a glucoside; and to water 7.67 per 
cent. of a very bitter extract, which has not yet been examined.

H. Helbing (Phar. Jour. and Trans., March 12, 1887, p. 747), has found the quality of 
the Kombé seeds to vary considerably; the best are 15 to 25 mm. long, and 4 to 5 
mm. broad, somewhat rounded at the base, narrowed at the apex and prolonged into 
the stalk of the hairy crown, somewhat twisted lengthwise, flattened, on one side with
a much more prominent keel-like ridge than on the other, of a grayish-green to brown color, and covered with appressed silvery silky hairs; 100 seeds weigh about 62 grains. Another variety of seeds is similar to the preceding in shape, but densely covered with loose, longer, silky, white hairs like a fur; 100 seeds weigh about 57 grains. The least heavy of the commercial strophanthus, seeds have a dusky, dirty color, the kernel is not white, the hairs of the crown are dingy yellow, and 100 seeds weigh about 33 or 34 grains.

On drying the Kombé seed at 120º F. they lose upwards of 5 per cent. of moisture, and give with ether 32.45 per cent. of dark green fixed oil, sp. gr. .925, and becoming brownish-red when heated on the water bath. The white strophanthus seed yielded 23.33 per cent. oil, which was a little paler in color, but otherwise like the preceding.

Mr. Helbing likewise found that the seeds freed from oil cannot be completely deprived of bitterness by the use of rectified spirit sp. gr. .838. A tincture thus prepared is of a very pale color, has the sp. gr. .840, and a fluid ounce of it yields about 120 mgm. of residue on evaporation. Three commercial tinctures had nearly the same density, but yielded respectively 88, 124 and 180 mgm. of residue. Four other tinctures were probably made with a weaker alcohol, were of a green or yellow color, varied between .870 and .900 in density, and yielded from 170 to 242 mgm. of residue.

H. D. Rolleston, B. A., (Ph. Jour. and Trans., March 19,1887, p. 761), observed that the ethereal extract of the seed gave with distilled water a solution, which on being filtered from the oil, had a bitter taste and the physiological effects of strophanthin. Similar results were obtained with the ethereal extract of strophanthus seeds prepared by different experimenters from white and green strophanthus seeds with absolute ether, showing that strophanthin is soluble in ether when the oil is present, and that the ethereal extract is not without value.

A. W. Gerrard, (Ph. Jour. and Trans., May 14, 1887, p. 923), obtained from strophanthus seeds by treatment with petroleum spirit, 31 per cent. of green fixed oil, and on subsequent treatment with 84 per cent. alcohol, 52 per cent. of extract. Using upon various samples of seeds successively petroleum benzin, ether and absolute alcohol, the latter yielded 5 per cent. of extract, or considerably more than had been obtained by Elborne. The alcoholic extract may be obtained without the costly process of percolation with ether; on boiling the ground seeds with alcohol, and distilling and evaporating the tincture, about 5 per cent. of hard extract is obtained, from which the 31 per cent. of oil can be easily poured off, and adhering traces be washed away with very little ether. Elborne's results of the absence of an alkaloid, ineine, from the comose hairs are confirmed.

Strophanthin was prepared from the alcoholic extract, by dissolving it in water, filtering, adding excess of tannin, washing the gray precipitate with warm water, mixing with excess of lead acetate, drying the mixture, exhausting it with warm alcohol, removing lead by H₂S, filtering and evaporating. Thus obtained, strophanthin is pale yellowish, amorphous, readily pulverizable, burns without residue, dissolves freely in water and alcohol, and is insoluble in absolute ether or chloroform. The watery solution, when shaken, gives much froth; warmed with silver nitrate the latter is reduced; tannin causes a white precipitate; on boiling with dilute sulphuric acid
Glucose is produced.

Helbing (ibid. p. 924), had observed that concentrated sulphuric acid dissolves strophanthin, changing, the color to dark green and finally dark reddish-brown. Minute traces of strophanthin may be detected by dissolving in a drop of water, adding a trace of solution of ferric chloride, and then a little concentrated sulphuric acid; a reddish-brown precipitate is formed which in the course of an hour or two turns emerald-green or a little darker-green, and this color remains unchanged for a long time.

Dr. F. F. Hanausek has published (Phar. Post, May 8, 1887, p. 301), a description of strophanthus seeds, from which the following abstract is made: Length of the seed 15 to 20 mm., width 4 mm., thickness about 1 mm., base rounded, apex attenuated to point which is prolonged into an awn almost 9 cm. long, the upper third of which is on all sides beset with delicate silky fragile hairs about 6 cm. in length. Seed yellowish-white, covered feltlike with soft silky hairs. The transverse section shows under the wrinkled testa a thin endosperm and two nearly plano convex cotyledons, the latter constituting the greater part of the seed. The section treated with potassa shows the testa colored golden-brown, the albumen colorless, and the cotyledons greenish or canary-yellow. Concentrated sulphuric acid colors the hairs and testa golden-brown, the albumen emerald-green, and the cotyledons yellow, changing successively to greenish, bronze-colored, coppery and finally almost blood-red. It appears from the reactions that the albumen contains principally fixed oil, and the embryo besides fat also strophanthin.

A false strophanthus seed has been examined by Mr. E. M. Holmes (Phar. Jour. and Trans., May 7, 1887, p. 903), and shown to be the seed of Kicksia africana, Bentham, which grows on the Bag rooriver, at Fernando Po and at Bonny, in open low country, and is the only known African species. The seed is without awn, but is attached to the long hairy funiculus, which resembles a retrorsely hairy awn. On transverse section the cotyledons are seen to be folded or contortuplicate. Prof. Birch isolated from the seed a toxic principle, which is not a glucoside, but most likely an alkaloid. Prof. Kickx, after whom the genus is named, was director of the Botanic Garden at Ghent, and president of the Botanical Society of Belgium, and died March 20, 1887.

These seeds, as figured by T. Christy (New Commercial Plants, part 10), are pointed at both ends, somewhat bent, not hairy, but the retrorse hairs of the funiculus project beyond the apex of the seed.

Other strophanthus seeds are also figured and described by Christy. The seed of Str. hispidus, De Cand., are smaller than Kombé seeds, dark brown, short-hairy, the bare awn rather short. Str. dichotomus var. Marckii, De Cand., from Java, has the seed rounded, but narrowed at the base, dark-brown, flat, slightly bitter; bare awn short, brown, the hairy portion paler and the hairs long. The seed of an unknown species, resembles Kombé, but is larger, gray-green, has a much longer awn, and is very bitter. Another seed from the Gold Coast is palebrown, scarcely bitter, the awn and awn-hairs rather short.

The seed of Str. Ledienii, Stein, (Gartenzeitung, 1887, p. 146; see also AMER. J O U R.
PHAR., 1887, p. 269), is of the shape and size of a wheat grain, densely covered with silky yellowish-brown hairs, and at the apex provided with an awn, which is about 2 cm. long, and from its base beset with hairs, the total length of the comose appendage being about 5 cm.

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ABSTRACTS FROM THE FRENCH JOURNALS
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LAMIUM ALBUM is thought by Dr. Florain, (Bull. Général de Thérap., June 15,) to be fully equal to the urticeae as a haemostatic. He claims great success with a preparation composed of the tincture, 100 gm., simple syrup 50 gm., and water 25 gm. Dose, a tablespoonful every half hour until the hemorrhage ceases; then, the same dose every few hours. Dr. Florain believes he has separated the active principle of the plant in the form of an alkaloid which he names lamine. His method of finding it was to treat 500 gm. of the stems gathered at the time of flowering, with hydrochloric acid and boiling water for half an hour. The liquor was treated with milk of lime and the precipitate extracted with boiling 80 per cent. alcohol. This was filtered and distilled to a syrupy consistence, when it gave, with sulphuric acid, a somewhat abundant white precipitate. This dissolved in boiling water gave, on cooling, long crystals "similar to those of sulphate of quinine." This substance dissolves in boiling water, is less soluble in alcohol, and has a neutral reaction. The alkaloid was given hypodermically, both as a sulphate and a hydrochlorate in somewhat high doses without toxic effects. The hemostatic effect of the alkaloid was promptly obtained. The writer hopes that analogous researches will be made with Urtica dioica and Urtica urens.