A PHYTOCHEMICAL STUDY OF KALMIA POLIFOLIA, ERICACEÆ.*

BY CLAIRE EVANS.**

INTRODUCTION.

Various Kalmia species of the family *Ericaceæ*, have from time to time evoked interest because of their plentifulness in some portions of this country and also because of cases of poisoning reported to be due to some of the species. These reports of poisonous properties of certain members of the genus Kalmia have, to a certain extent, cast suspicion upon all members of the genus.

Although the Kalmias are not official, either in the United States Pharmacopœia or in the National Formulary, they are mentioned in the United States Dispensatory (1), and some of the plants have been used medicinally.

Kalmia latifolia and *Kalmia angustifolia* are the species which, up to the present time, have been the subject for most of the investigative work. Since, as far as could be ascertained, no experiments had been carried out on *Kalmia polifolia*, and since the plant grows fairly abundantly here in the Pacific Northwest, it was deemed of interest to investigate the species from a botanical, chemical and toxicological standpoint.

HISTORICAL—PHYSIOLOGICAL ACTION AND USES OF THE GENUS KALMIA.

Kalmia latifolia has long been considered a poisonous plant (2), and has been stated as the cause of poisoning in cows, horses, sheep, goats and chickens. Dr. R. H. Stabler (3), Cary and Mathews (4), as well as Crawford (5), testify to the poisonous results obtained from experimental feeding of this plant. The Dispensatory (1) states that the leaves of *Kalmia latifolia* have been used internally for diarrhoea and for syphilis, and externally for skin diseases.

Kalmia angustifolia has also long been considered a poisonous plant. In fact one of its common names, Lambkill, owes its origin to the plant's reputation for being fatal to sheep. Chesnut (6) states that many fatalities have been caused by *Kalmia angustifolia*. According to the Dispensatory (1), a decoction of the leaves of this plant is used by the Negroes as a wash for ulcerations between the toes.

Kalmia microphylla, when fed experimentally to range animals, was claimed by Fleming (7) to cause poisoning.

Kalmia polifolia (Wang) or *Kalmia glauca* (Ait), also known as Swamp Laurel, is a species belonging to the same genus and family as the above plants and served as the subject for the experimental work reported in this paper. It grows in sphagnum bogs from Newfoundland to Alaska, in the Rocky Mountains and various other localities. Although no definite cases of poisoning are cited, Pammel (8) states that *Kalmia polifolia* is poisonous.

CHEMICAL WORK DONE ON KALMIA SPECIES.

Kalmia latifolia when investigated by Bullock (9), gave no evidence of a volatile oil. Kennedy (10) claimed the isolation of arbutin from this plant, while Plugge (11) named it as a source of andromedotoxin. A glucoside, called at first

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kalmifoliin, was obtained from *Kalmia latifolia* by Bourquelot and Fichtenholz (12), but this was later shown by these investigators to be identical with the glucoside asebotin, isolated in 1883 by Eykmann (13) from Andromeda japonica. Bridel and Kramer (14) isolated the glucoside asebotin from *Kalmia latifolia* and compared its properties with those of phloridzin, while Verdun (15) made a study of the pectin of *Kalmia latifolia*.

Kalmia angustifolia was thought by Deibert (16) to contain arbutin, as well as wax, resin and fixed oil. This species also was listed among the andromedotoxin bearing plants by Plugge (11).

EXPERIMENTAL.

The *Kalmia polifolia* used in this work was gathered from the Ronald bog a few miles north of Seattle during the months of June, July and August. For the chemical work the leaves and stems were carefully separated and dried in air.

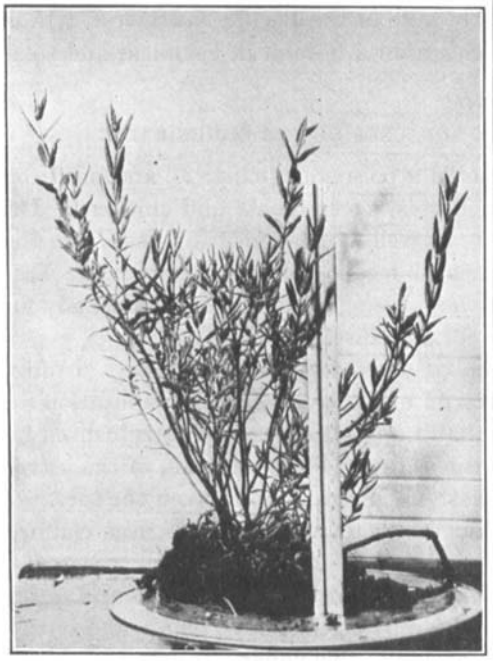

Plate I.—Entire plant of *Kalmia polifolia* beside a 12″ scale.

Plate II.—Branch of *Kalmia polifolia* showing capsules.

A. BOTANY.

The Plant.—Plate I shows the entire plant of *Kalmia polifolia* beside a 12-inch scale. The plant is an evergreen shrub usually from 30–60 cm. high. Plate II illustrates a branch of *Kalmia polifolia* bearing dry capsules. These capsules are 5-celled, many-seeded and arranged in corymbs. The flowers which precede these capsules have a purple corolla 12–18 mm. broad, 5-lobed; calyx 5-parted. The leaves are seen to be opposite, oblong, entire, with revolute margin, shiny green above and glaucous beneath.

Microscopic Study of the Leaf.—The general outline of the leaf in cross section appears in the form of a figure three, due to the curling of the leaf edges and prominence of the midrib on the under side. The glaucous appearance of the lower part of the leaf, as seen with the naked eye, is

found upon microscopical examination to be due to the numerous trichomes which project from the lower epidermis. In fact, when the lower epidermis is stripped from the leaf, and observed under the microscope, it appears to be only a mass of these projections. With exception of the few trichomes that occur along the midrib of the upper surface of the leaf, the upper part of the leaf is perfectly smooth, shining and possessed of a very thick cuticle. Beneath the upper epidermis occur from one to two rows of palisade cells below which is the spongy parenchyma.

The midrib, in cross section, has a lower epidermis protected by a thick cuticle without trichomes. Next to this lower epidermis there appears a supporting band of sclerenchyma, beneath which occur the large thin-walled cells of the cortical region. The vascular tissues of the midrib are arranged in the form of a fan, and are almost completely surrounded by large, heavy-walled sclerenchyma cells.

Microscopic Study of the Stem.—The stems of the younger plants are soft and green, while those of the older plants are hard and woody. A cross section of a young stem exhibits an epidermis with heavy cuticle and occasional trichomes. The web of parenchyma cells forming the cortex widens on two sides of the stem, thus giving the latter a lemon-like outline when viewed transversely. A circle of small cells, usually one or two in width, occurs at the inner boundary of the cortex. Within this circle of cells appear the vascular tissue and a large web of pith.

A small portion of woody stem, upon maceration according to the method of Jeffrey and examination under the microscope, showed wood fibers from 0.3 to 0.5 mm. in length, pitted tracheids from 0.3 to 0.4 mm. in length, parenchyma cells, spiral vessels and vessels having cross markings.

B. CHEMISTRY.

Various preliminary analyses were made. Alkaloid (17) and ash (18) determinations were carried out by the U. S. P. X method, while tannins (19), sugars (20), starch (21) and pentosans (22) were assayed according to the A. O. A. C. For ascertaining the total pectic substances present in the leaves, the procedure of Caré and Haynes (23) was used. The results, stated in percentages, were as follows:

Freshly Picked Material.	Leaves.	Stems.
Loss of weight at 100° C.	57.3	14.43
Air-Dried Material.		
Ash	3.44	1.42
Tannins	12.96	1.95
Sugars (as glucose)	1.77	0.35
(after inversion)	2.26	2.01
Starch	0.92	1.57
Pentosans	4.58	20.46
Pectins (as calcium pectate)	2.40	...
Alkaloid	0.00	0.00

The amount of volatile oil derived by ether extraction of the steam distillate from 26.179 Kg. of fresh leaves was practically negligible. Volatile oil is present, therefore, only in traces in both the leaves as well as in the stems, as is shown later by steam distillation of an alcoholic extract prepared from the stems.

SELECTIVE EXTRACTION.

A five-Gm. sample of the air-dried, powdered leaves was extracted in a Soxhlet apparatus for twenty-four hours with petroleum ether. After evaporation of the solvent from the thimble, the same sample was successively treated in a similar manner with ether, chloroform, absolute alcohol and finally with water. The solvents were allowed to evaporate from the extracts spontaneously, after which the extracts were dried to constant weight first at 100° C. and then at 110° C.

The above process was repeated using a five-Gm. sample of dried, powdered stems. The results for both leaves and stems appear in the following table. The percentages are based on the weight of the original sample taken.

TABLE I.—SELECTIVE EXTRACTION. PER CENT OF EXTRACTIVE.

Leaves.	At 100° C.	At 110° C.
Petroleum ether	2.61	2.56
Ether	4.60	4.59
Chloroform	2.33	2.29
Absolute alcohol	14.73	14.70
Water	11.53	11.50
Stems.	At 100° C.	At 110° C.
Petroleum ether	1.22	1.21
Ether	0.81	0.81
Chloroform	0.46	0.42
Absolute alcohol	5.03	4.96
Water	7.24	7.12

EXAMINATION OF AN ALCOHOLIC EXTRACT OF THE LEAVES.

Thirteen hundred grams of dried, powdered leaves were extracted repeatedly with hot alcohol. The alcoholic extracts were combined, filtered and the solvent was removed by vacuum distillation. The extract so obtained amounted to 332.1 Gm. of a dark, sticky material from which the water-soluble materials were removed with boiling water. A combination of these aqueous washings formed what is designated below as the aqueous liquid (A). The original alcoholic extract thus became divided into two portions, *i. e.*, a water-soluble portion (A), and an insoluble greenish resinous mass (B), which on drying in air amounted to 92.3 Gm.

Examination of the Aqueous Liquid (A).—Concentration and cooling of the aqueous liquid (A) caused separation of a dark brown mass of material containing crystals which were washed with cold water and recrystallized from hot water. This substance proved to be the glucoside asebotin, identified elsewhere in a later part of this work.

The remaining solution (A) gave distinct tests for tannin with ferric chloride, strychnine nitrate, gelatin and egg albumen.

The original aqueous solution, after separation of the glucoside, was shaken with ether, which in turn was extracted with aqueous ammonium carbonate. The carbonate solution after acidification was again extracted with ether, which upon evaporation yielded only a negligible quantity of indefinite material.

Examination of the Leaf Resin (B).—The crude, resinous, water-insoluble material which had been separated from the aqueous liquid (A), as previously described, was mixed with a large proportion of pure quartz sand and extracted in a Soxhlet apparatus with various solvents, when the following amounts of extract, dried at 100° C., were obtained:

Petroleum ether extracted	20.8 Gm. or 1.6%
Ether extracted	32.1 Gm. or 2.5%
Chloroform extracted	12.4 Gm. or 0.9%
Alcohol extracted	23.5 Gm. or 1.8%

The percentages are based on the weight of the original dried leaves taken. Each of the above extracts was examined in turn.

Petroleum Extract of the Leaf Resin (B).—This dark green extract, after dissolving in ether and extracting with solutions of ammonium carbonate, sodium carbonate and sodium hydroxide from which nothing definite was obtained, was freed of ether and saponified with alcoholic potassium hydroxide. An ethereal extract from the soapy mixture yielded, on evaporation, a yellow mass containing carotinoids from which the desired compound was precipitated by the addition of a warm alcoholic solution of digitonin (24). The white precipitate obtained was then refluxed with xylol for eighteen hours in order to dissolve out the sterol. Removal of the xylol left a white crystalline residue which, after recrystallization from hot alcohol, melted at 128.5° C., and responded to the color tests for phytosterol.

Ethereal Extract of the Leaf Resin (B).—Further purification of this material showed it to contain a grayish powder which melted indefinitely around 202° C. It gave the color reactions

for sterols, and appeared to be an impure mixture of the sterol found later in greater amount in the chloroform fraction.

Chloroform Extract of the Leaf Resin (B).—The addition of chloroform to this brown extract caused the separation of a grayish white powder. This powder, upon drying proved to be non-crystalline and melted around 244° C. Numerous attempts made to crystallize the material from various organic solvents, such as alcohol, ethyl acetate, chloroform, benzol, ether, petroleum ether, pyridine or mixtures of these, resulted only in a gelatinous mass instead of crystals; nor did the addition of varying amounts of water to an alcoholic or pyridine solution yield the desired result. After repeated treatment with the above-mentioned solvents, the melting point of the material was finally raised to 250–255° C.

The powder under observation proved to be quite soluble in cold chloroform, pyridine, acetone, amyl alcohol and in ethyl acetate. It was only slightly soluble in cold alcohol or xylol, but much more soluble in the boiling solvents. Benzol, ether, petroleum ether, methyl alcohol and glacial acetic acid showed only a slight solvent action, while 5 per cent sodium hydroxide solution, cold 70 per cent acetic acid or boiling water had no solvent action upon the material.

The above substance gave negative tests for sulfur, nitrogen, aldehydes, ketones, phenols and carbohydrates.

Tests for Phytosterol.—A sample of the solid when dissolved in acetic anhydride, and mixed with a few drops of concentrated sulfuric acid, produced a beautiful reddish violet color which changed to blue, green and finally brown. The color reaction of Salkowski was positive after placing the test-tube for a short time in warm water. Positive color reactions were obtained by Schiff's test and by the iodine-sulfuric acid test. No precipitation occurred, however, upon the addition of a saturated solution of digitonin in 90 per cent alcohol, to a saturated alcoholic solution of the powder under investigation.

Acetylation.—A 0.1-Gm. sample was boiled with acetic anhydride, after which the mixture was subjected to crystallization from alcohol. Rosettes of crystals formed, which after washing with chilled alcohol, became white and melted sharply at 274° C. These crystals after heating with normal alcoholic sodium hydroxide for 30 minutes, diluting with three volumes of water and standing over night formed crystals which melted at 225° C. and gave the color reactions of the phytosterols.

Phytosterolin.—Power and Salway (25) have shown that some of the phytosterols can be hydrolyzed to glucose. These have therefore been designated as phytosterol glucosides or phytosterolins. Consequently, the sample was refluxed for three hours on a steam-bath in the presence of dilute hydrochloric acid and enough amyl and ethyl alcohols to make a homogeneous liquid. Subsequent to removal of the organic solvents, the water-insoluble material was filtered off and recrystallized from alcohol, when it melted at 272° C., and gave the color reactions of the phytosterols.

The above aqueous filtrate, after neutralization and concentration, caused no reduction when heated with Benedict's solution. This phytosterol is therefore not a phytosterolin since it does not hydrolyze to a reducing sugar.

Treatment with Alcoholic Sodium Hydroxide.—A 2.4-Gm. sample of the original powder obtained from the chloroform extract was heated for half an hour with 48 cc. of alcoholic sodium hydroxide solution. Upon the addition of 120 cc. of boiling water, shaking and allowing to stand for a few minutes, a mass of crystalline needles formed. Because of difficulties encountered in filtration, and also when using organic solvents, the crystals were centrifuged repeatedly with fresh portions of cold 20 per cent alcohol, and then several times with cold distilled water until the washings were neutral. When separated and dried, the snow-white, crystalline substance melted at 236° C. and gave the color reactions for the phytosterols but did not, however, precipitate with digitonin. A sample of these crystals dried to constant weight both over sulfuric acid, and in a vacuum oven at 92° C., gave an analysis C—71.9 per cent, H—10.4 per cent.

The simplest empirical formula corresponding to this percentage composition would be $C_{11}H_{19}O_2$. The empirical formula $C_{23}H_{38}O_4$ given for citrullol, which has been isolated from colocynth (26), Euonymus atropurpureus (27), and caulophyllum thalictroides (28), also corresponds to the latter percentage composition. Citrullol also gives the color reactions for the phytosterols, but the melting point of Citrullol has been given as varying anywhere from 275°–290° C., while its acetyl derivative melts between 164°–170° C. Citrullol also differs in that it

hydrolyzes to sugar (19) while the sterol from *Kalmia polifolia* yielded negative results when so treated. It is therefore probable that the sterol from *Kalmia polifolia* is not identical with Citrullol nor, as far as could be ascertained, with any other substance which has ever been studied.

Alcoholic Extract of the Leaf Resin (B).—This black shining, brittle, nearly tasteless material, after repeated extraction with warm ethyl acetate, yielded no deposit of crystals on concentration of the ethyl acetate solution.

EXAMINATION OF AN ALCOHOLIC EXTRACT OF THE STEMS.

This examination was carried out in a similar manner to that which was performed on the leaves. A quantity of dried, powdered stems weighing 6500 Gm., after repeated treatment with hot alcohol, gave 410.1 Gm. of a brownish extract upon removal of the alcohol. Distillation of this alcoholic extract with steam and subsequent extraction of the steam distillate with ether yielded less than one cc. of a yellowish sharp smelling oil.

There remained in the distillation flask, after distillation of the extract with steam as above described, a brownish liquid (A), and a quantity of somewhat greenish resinous material (B). These products while still hot were separated by filtration, and the resin was washed thoroughly with hot water and dried.

Examination of the Aqueous Liquid (A).—The aqueous liquid, on cooling, deposited a gummy indefinite residue, but yielded no crystalline mass of glucoside, as was obtained at this stage during the examination of the leaf extract. Nothing definite was obtained from the aqueous stem extract upon treatment with amyl alcohol or ether.

Examination of the Stem Resin (B).—The dried resinous material which had been separated from the aqueous liquid (A) as previously described, was mixed with purified quartz sand and extracted successively in a Soxhlet apparatus with various solvents. The weights of the products obtained dried at 100° C., were as follows:

Petroleum ether extracted	48.9 Gm. or .75%
Ether extracted	26.1 Gm. or .40%
Chloroform extracted	2.8 Gm. or .4 %
Alcohol extracted	124.5 Gm. or 1.9 %

The percentages are based on the 6500 Gm. of the original dried stems taken.

The above, dark green, fatty petroleum-ether extract after having been taken up in ether, and washed with an aqueous solution of sodium hydroxide, finally yielded a substance which gave the color reactions for the phytosterols. Crystals melting at 128.5° C. were obtained by treatment of the material with boiling 90% alcohol. A mixture composed of the phytosterol from the leaf which melted at 128.5° C. and the phytosterol from the stem showed no depression of the melting point. It would, therefore, appear that these two are identical.

The ether and chloroform extracts from the stem resin (B), yielded nothing definite when treated with solutions of ammonium carbonate, sodium carbonate or sodium hydroxide. No crystalline material was obtained from the dried alcoholic fraction of the stem resin after repeated treatment with hot ethyl acetate.

GLUCOSIDE.

A concentrated, aqueous extract prepared from 3985 Gm. of dried, powdered leaves of *Kalmia polifolia* was digested with hot alcohol in order to take up any glucoside present. Purification of the glucoside from the alcoholic extract was accomplished by exhausting the latter with acetone. Treatment of the residue which remained after evaporation of the acetone with hot water, and removal of foreign materials with lead acetate and hydrogen sulfide, brought about a display of groups or rosettes of many needle-shaped, nearly colorless, crystals which separated from a concentrated, hot, aqueous solution. The yield of these bitter tasting crystals amounted to 16.27 Gm., or 0.4 per cent of the weight of the leaves taken.

The crystalline material under observation dissolved only sparingly in cold water, about 0.06 Gm. dissolving in 100 cc. It dissolved readily in hot water, sodium hydroxide, alcohol and in acetone. The crystals were amost insoluble in ether, chloroform, ethyl acetate or petroleum ether.

The specific rotation of a solution in alcohol at 50° C. was −54.2°. The crystals themselves melted at 137.5° C., but upon hydrolysis with sulfuric acid, there was obtained by extraction of

the liquid with ether, a crystalline substance which melted at 163° C. The hydrolyzed glucoside also reduced Benedict's solution. After separating off the ether-soluble substance, obtained by the above hydrolysis, the remaining aqueous solution was neutralized with barium hydroxide, and filtered. A portion of this filtrate gave a negative test for fructose when boiled with Seliwanoff's reagent. An osazone melting at 204° C. and resembling that of dextrose was prepared from the above filtrate by means of phenylhydrazine hydrochloride.

The glucoside gave a decided Molisch reaction. Concentrated nitric acid put on the dry glucoside gave first a black color, turning deep purple, and finally reddish brown. The crystals, when evaporated on a steam-bath with concentrated nitric acid, gave finally a brownish red color. When the glucoside was moistened with water and inverted over a dish containing 10 per cent ammonia water, a yellow color was produced, which changed to reddish brown. Bromine water with a solution of the glucoside gave a white turbidity. Saturated solution of normal mercurous nitrate, when added to a solution of the glucoside, caused a pink coloration, especially if allowed to stand; while with more concentrated solutions of the glucoside, a red color was obtained. Sometimes when this test was performed the mixture became turbid on standing, while at other times the mixed solutions remained clear but gelatinized after a time. Mercuric nitrate solution when added to a solution of the glucoside gave a slight white turbidity. This mixture, in time, became gelatinous. Frohde's reagent, when added to the crystals, gave a blue color, changing to green and finally to brown. Ferric chloride, when added to a solution of crystals, gave a reddish brown color.

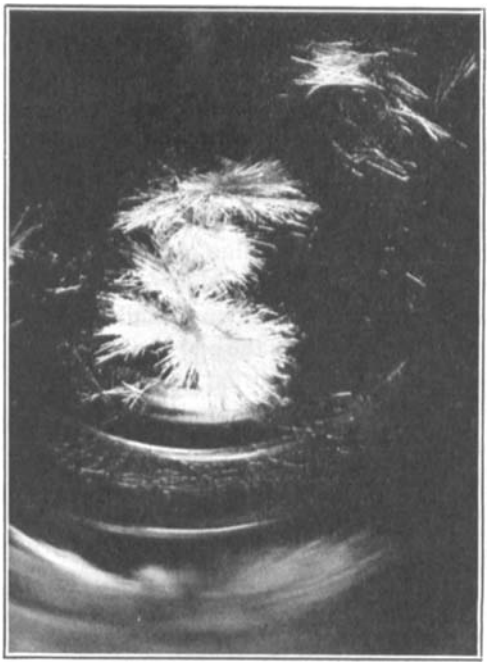

Plate III.—Glucoside, asebotin, from *Kalmia polifolia* leaves. Natural size.

Jungmann's Test.—When the glucoside was dissolved in water, made alkaline with ammonia, and a solution of phosphomolybdic acid added, a blue color was produced.

The foregoing tests correspond to those of the glucoside asebotin found in the leaves of *Andromeda japonica* by Eykmann (13), and isolated also from the leaves of *Kalmia latifolia* by Bourquelot and Fichtenholz (12), and later studied by Bridel and Kramer (14).

It is probable that the arbutin which Deibert (16) claimed to have isolated from *Kalmia angustifolia*, and which Kennedy (10) claimed to have obtained from *Kalmia latifolia* was really asebotin, since these workers based their identification of the substance isolated on Jungmann's test, and asebotin also gives this reaction.

A sample of dried powdered stems weighing 200 Gm. was extracted like the leaves in order to ascertain the presence of the above glucoside. However, no glucoside was obtained. It would seem, then, that this glucoside is not present in the stems, since it was not obtained either during this experiment nor after steam distillation of the alcoholic extract of the stems, although it is possible to obtain the glucoside from the leaves even after steam distillation.

TOXICOLOGY.

Since *Kalmia polifolia* was thought to be poisonous (18), experiments were carried out on animals, in an attempt to settle the question of its toxicity. It was found impossible to get the rabbits and white rats used in the experiments to eat the fresh leaves, although all other food was withheld for two days. The rats likewise refused a mixture composed of the dried powdered leaves with their regular diet. As a result various extracts were finally made, rolled into pellets

and forcibly fed to the animals. From 0.1 to 0.3 Gm. of pilular alcoholic extract (each Gm. of which represented 4.1 Gm. of dried leaves) was fed to two white rats, weighing around 150 Gm. each. One gram of this extract was also fed to a rabbit weighing 1872 Gm. A rat weighing 148 Gm. and a rabbit weighing 1984 Gm. were fed 0.3 Gm. and 1.0 Gm., respectively, of an aqueous extract, each Gm. of which represented 7.9 Gm. of dried leaves. Ether, chloroform and benzol extracts were also fed to the rats, as well as a 0.12-Gm. dose of the glucoside asebotin. In no case did any of the above extracts nor the glucoside produce poisonous symptoms.

SUMMARY.

The plant material employed consisted of the carefully separated leaves and stems of *Kalmia polifolia*, grown in the Pacific Northwest.

During the botanical work, paraffin sections both of the leaves and of the stems were made, examined microscopically, and then photographed.

Both the leaves and the stems, when investigated separately, were found to contain sugars and tannins. The pectins were extracted from the leaves and examined. Steam distillation yielded from the leaves as well as from the stems only a trace of volatile oil. Neither the leaves nor the stems gave positive tests for alkaloids when extracted according to the pharmacopœial method and treated with alkaloidal precipitants. From the water-insoluble portion of the acoholic extract of the leaves, two substances were obtained which yielded the color reactions for phytosterols, one melting at 128.5° C., which precipitated with digitonin, and the other melting at a much higher temperature (250–255° C.) which did not precipitate with digitonin. The stems yielded only one phytosterol which gave the same tests and melting point as the one from the leaves which melts at 128.5° C. The glucoside asebotin was found to be present in the leaves but not in the stems.

As to the toxicity of the leaves, various extracts prepared from them by the use of water, alcohol, chloroform, ether and benzol produced no poisonous symptoms when fed experimentally. Oral introduction of the glucoside also was without toxic effect.

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PRELIMINARY STUDIES OF THE BOTANICAL COMPONENTS OF TECUNA AND JAVA CURARE.*

BY KARL FOLKERS.

Curare, the arrow poison of the South American Indians, is composed of the combined extractives of many toxic plants. The curares of natives of different geographical locations vary in preparation, composition, physiological action, etc. The differences in action are no doubt primarily dependent upon what species of the genera of toxic plants are accessible and are used by the natives in each locality. There has been much scientific study, for many years, of the active principles of the curares. The two basic approaches to the study of these active principles are: *First*, studies starting with native curares, and *second*, studies starting with the botanical components. Certain recent studies involving both methods are those of H. King (1, 2, 3), Ranyard West (4, 5, 6), Wieland, *et al.* (7), Späth (8), Friese (9), Hauschild (10) and Santesson (11).

This paper is a contribution to the knowledge of curares as based on the second approach; that is, a study of the botanical components. B. A. Krukoff, on his Sixth Expedition to Brazilian Amazonia during 1935 and 1936, secured authentic crude material, backed by herbarium specimens, which was used by the Tecunas and Javas in the preparation of their arrow poison. Notes on the botanical components of these two curares were published by Krukoff and Smith (12). The preliminary chemical and pharmacological studies on this plant material, as herein described, were made from the point of view of determining which plants contained alkaloids of paralyzing action, and which ones did not. This selection, made upon authentic botanical material, would provide a basis for further studying the active principles of these curares as obtained from certain species of plants.

It seemed desirable to test first an extract of each plant material which would represent the total alkaloids. Since the "curarines" have been generally recognized to be quaternary ammonium bases, then this first extract should contain the qua-

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