

of these influences are possible to exist at any moment of time within the area of the United States?

Here $n=8$; $r=3$; then, $n-r+1=4$.

Employing the general formula for combination,

$$\frac{n(n-1)(n-2)\dots(n-r+1)}{r}$$

Or $\frac{8 \times 7 \times 6 \times 5 \times 4}{1 \times 2 \times 3 \times 4 \times 5} = 56$ possible combinations.

And if the variations of temperature from 10 degrees Fahr., and atmospheric moisture from 0 to 100 percent, were extended through the twenty-four hours of the day, and included in our calculation, the number of permutations and combinations would reach an inconceivable number.

While there may be no perceptible change effected by these minute variations, their influences are nevertheless constantly at work, seeking to break down the molecular structure of chemical compounds.

Heat, for example, is most effective in releasing the gaseous NH_3 and CO_2 from Ammonium Carbonate, causing that compound to lose its characteristic translucent appearance and take on that of an opaque body, changed in its chemical constitution from a carbonate to a bicarbonate.

What has been written in the preceding pages contains the elements of an important research—its magnitude precludes the possibility of individual achievement, and its successful accomplishment will depend upon the cooperation of a number of qualified men, willing to work.

ON CRYSTALLINE KOMBE'-STROPHANTHIN.

D. H. BRAUNS, PH. D., AND O. E. CLOSSEN, PH. B., DETROIT, MICH.

Commercial *Strophanthus Kombe* seed has frequently been found to contain seeds of different *Strophanthus* species. Mr. E. M. Holmes, F. L. S., the curator of the museum of the Pharmaceutical Society of London observes,¹ "The *Strophanthus* leaves on the table were presented to the society's Herbarium some months ago by Mr. Lindsay, the curator of the Edinburgh Botanical Garden. They had been grown from some of the seed, used by Professor Fraser, apparently the greenish brown kind. These leaves differed considerably from those specimens of *Strophanthus Kombe* in the Kew Herbarium, so that it appeared, they were derived from a hairy leaved species, resembling *Strophanthus hispidus*, but not identical with it."

Twenty-two Kg. *Strophanthus Kombe* fruit (seed in pods) in very good condition were identified by Mr. Holmes of London as true *Strophanthus Kombe* Oliv. seeds. This statement is of great value, as there are more than twenty-nine

¹The *Pharmaceutical Journal and Trans.*, 1887, 17, p. 754 and p. 755, also 1889, 20, p. 335.

species of *Strophanthus*.² The chemistry of *Strophanthus* seed Kombe and in particular that of strophanthin is in an uncertain state due possibly to the fact that the strophanthin under examination was prepared from seeds other than the Kombe species, but generally to other causes, as will be shown. Commercial strophanthins vary considerably in their chemical reaction as well as their physiological activity.

To clear up these uncertainties and to determine whether a strophanthin of constant chemical, physical and physiological properties can be prepared, is the object of the experiments described in this paper. It includes also a summary of the most interesting work done on strophanthin and the methods for its preparation used by the different investigators with an account of the origin and characteristics of the seed used. A complete list of the chemical literature on Kombe-strophanthin (including gratus-strophanthin or ouabain³ and hispidus strophanthin) is given at the end of the communication.

Fraser⁴ was the first investigator to obtain an active principle which he called strophanthin from *Strophanthus* seed.

Some of the seeds, which Fraser used, were of a species resembling *Strophanthus hispidus*, but not identical with it.

Fraser's method for obtaining strophanthin was changed several times. The first process on which he based the second one is not accurately reported, as pointed out by Gerrard⁵. The first process seems to have been an extraction with alcohol, and a precipitation of the active principle with ether. The second process is as follows: The ether precipitate obtained in the earlier process is dissolved in water, tannic acid is added and then digested with recently precipitated oxide of lead. The digested material is extracted with alcohol and the solution precipitated by ether. The precipitate is finally dissolved in weak alcohol and through this solution carbon dioxide is passed for *several hours*, by which means the lead is completely removed. After filtration, the solution is evaporated at a low temperature and dried in vacuo over sulphuric acid.

The third process is the following: The powdered seeds were extracted with sulfuric ether, afterwards with 20 times their weight of rectified spirit. The spirit was distilled off. The active principle was precipitated by a solution of tannin from a strong solution of the extract in water; the well washed tannate was thoroughly mixed with recently precipitated, carefully washed and moist

²Holmes, *The Pharmac. Journal and Trans.*, 1893, 23, p. 868 and p. 927. Hartwich, *Archiv. der Pharm.*, 1892, 230, p. 401.

³The following is a quotation from a publication of Hatcher and Bailey: "The clinical use of *Strophanthus*" in the *Journal of the American Medical Association* (Vol. 55, 1910, p. 1698): "Even such closely related bodies as strophanthin and crystalline ouabain, strophanthin being methyl-ouabain, show different ratios of activity by subcutaneous and intravenous injections into the cat—." Because Strophanthin of the Pharmacopoeia of the U. S. is Kombe-strophanthin, we are sure that the strophanthin Hatcher and Bailey refer to, must be Kombe-strophanthin. But then their statement cannot be true. As far as our knowledge goes about ouabain (or gratus strophanthin) this body has the formula $C_{30}H_{46}O_{12} + 9H_2O$, and it is hydrolyzed according to the equation:

$$C_{30}H_{46}O_{12} + H_2O = C_6H_{12}O_5 + C_{24}H_{34}O_7$$

$C_6H_{12}O_5$ being rhamnose anhydride (Arnaud, *Comptes rendus* 126 (1898), p. 1203). By the work of Feist, which is confirmed in this work, we know that Kombe-strophanthin is hydrolyzed to strophanthidin of the formula $C_{27}H_{38}O_7$. Without saying more about the properties of the cleavage product of ouabain (or gratus-strophanthin) it will be clear that the statement that "Kombe strophanthin is methyl-ouabain," which is to be found in literature (Arnaud, *Comptes rendus* 107, 1888, p. 179, also Kohn and Kulisch *Monatshfte* 19, 1898, S. 385), cannot be true.

⁴The *Pharmaceutical Jour. and Trans.*, 1873, 3, p. 523, 1887, 18, p. 69, 1889, 20, p. 206 and p. 328.

⁵The *Pharmac. Jour. and Trans.*, 1887, 17, p. 923.

oxide of lead, which was added in a quantity calculated to be necessary for the conversion of the tannin into tannate of lead; the mixture was digested for several days at a low temperature, and after it had been dried, it was thoroughly exhausted with alcohol. The alcoholic solution was generally evaporated to a syrupy consistence and repeatedly treated with oxide of lead until every trace of tannin had been removed. The product was now dissolved in dilute alcohol and any sediment removed by filtration, and through the clear and usually almost colorless solution a gentle stream of well-washed carbonic acid was passed *for two or three days*⁶ in order to remove traces of lead. The solution was then evaporated to dryness, and the residue dissolved in alcohol and filtered. Ether was added to the filtrate to precipitate the active principle. The precipitate was dissolved in absolute alcohol, which usually left a further slight sediment and the clear alcoholic solution was finally dried by being placed in a partial vacuum over sulphuric acid. Strophanthin thus obtained is a colorless opaque and brittle substance, which, under the microscope is found to consist of minute irregular crystalline plates. Strophanthin is intensely bitter and in solution in water or alcohol *is acid in reaction*. It melts at a temperature of (343° F.) 173° C. It burns without leaving a residue and contains no nitrogen. Strophanthin is decomposed by dilute acids yielding crystalline strophanthidin, and a syrup, (acc. to Fraser glucose), which reduces Fehling's solution. The results of the combustion and its reaction with H₂SO₄ will be given later in the table.

Arnaud. The communication of *Arnaud*⁷ is short yet interesting for our purpose; (a translation of the chemical part is as follows): The Strophanthus Kombe seeds in very good condition were furnished by Thomas Christy of London. The following is the method of preparation. The seeds pulverized in the mill are extracted, using a reflux condenser with boiling 70% alcohol. After boiling some hours, the extraction is completed in a percolator. The alcoholic fluids are distilled on the waterbath to remove most of the alcohol, the distillation being finished in vacuo, leaving a certain amount of fluid. The oil floating on the top of the cooled extract is separated and the remaining fluid filtered. A small amount of a mixture of subacetate of lead and finely-powdered litharge is added, heated on the waterbath and filtered after cooling. The lead in solution is eliminated by hydrogensulphide and the clear fluid is concentrated at 50° to a thin extract. In twenty-four hours strophanthin will crystallize out. The crystals are filtered off, keeping the temperature at 50°. If the fluid is not too concentrated, the syrup can be separated by filtering and by placing the crystals on unglazed porcelain. The crystals can be purified by recrystallizing several times from *boiling water*.

The yield of crystallized Kombe-strophanthin is 4.5 gm. from 1 Kg. of seed, but a part of the strophanthin is kept in solution in the syrup. It is perhaps possible to recover this strophanthin by making the tannate.

Properties. Strophanthin is a white substance, very bitter, crystallizes in brilliant crystals grouped around a center of micaceous appearance, resembling cadmium iodide especially when suspended in water. These crystals are very porous

⁶Compare the preceding process.

⁷Comptes rendus, 1888, 107, p. 179.

and hold the water back easily. Strophanthin⁸ forms a hydrate, which melts below 100° and loses its water in vacuum. By trying to recrystallize it, we find that the substance has become uncrystallizable, but if the substance is completely dehydrated in vacuo, it can be heated to 110° without alteration.

Strophanthin gives no residue when burned in the air. It has no sharp melting point, but softens at 165°, losing its opaqueness and quickly becoming brown. It acts on polarized light in watery solution (concentration 2.3%); (α)_D = +30°.

Cold water dissolves strophanthin slightly, 1 part to 43 parts of water 18° C. It is readily soluble in alcohol. It separates out of alcohol as a resin. It is insoluble in sulphuric ether, carbon disulphide and petroleum ether. Tannic acid precipitates it out of water solution. Strophanthin does not contain nitrogen. (The results of the combustion will be given in the table.)

*Leopold Kohn and Victor Kulisch*⁹. The seeds used by these authors to prepare strophanthin were examined by Hartwich, who declared the seeds to be identical with, or at least closely resembling the seeds used to prepare the strophanthin with which Feist made his experiments and which were said to be Kombe seed.

The strophanthin of Kohn and Kulisch was compared with the strophanthin of Merck, which was prepared from hispidus seed. The preparations were found to be identical.

The method of preparation of Kohn and Kulisch is the same as that of Arnaud. The seeds were freed from comose hair and pounded, extracted in a Soxhlet apparatus with petroleum ether to remove the fatty oil, afterwards dried and is washed until the acid reaction disappears and is recrystallized several times then extracted with 70% alcohol. The filtered alcoholic extracts were precipitated with basic lead acetate and lead hydroxide and filtered. The filtrate was treated with hydrogen sulphide and filtered again. From the filtrate concentrated in vacuo the strophanthin separates out. Recrystallization from water proved to be the best method for purifying the product.

Properties. Under the microscope the preparation shows crystalline structure. It is white, of neutral reaction and does not contain nitrogen. It does not reduce Fehling's solution in the cold or by heating and is optically inactive or slightly levorotatory. Strophanthin is very hygroscopic. The water is hard to remove from strophanthin, which melts at 100° C. It is not easy to determine the melting point of strophanthin, the mean of several estimations for the carefully dried strophanthin is 179° C. (The results of combustion, other estimations and adopted formula of strophanthin will be compared later on in a table.)

When strophanthin is boiled with diluted acids a new insoluble crystalline body *strophanthidin* is formed and the filtrate reduces Fehling's solution.

Melting point, etc. (see table). The method of preparation of strophanthidin is as follows: 10 gm. strophanthin were dissolved in 200 cc. water and heated with 20 cc. HCl of spec. grav. 1.12 in a large flask with reflux condenser. When the fluid starts to boil the impure strophanthidin separates in fine yellow flakes. After heating fifteen minutes the fluid is cooled and filtered. The strophanthidin

⁸The following is interesting as will be shown afterwards.

⁹Berichte 31, p. 514, and Monatshefte f. chemie, 19, p. 385.

from hot alcohol. The final product appears in the form of fine white silky needles. Strophanthin cannot be dried at 100°, as it is decomposed at this temperature.

Kohn and Kulisch also prepared strophanthin by the method which Hardy and Gallois¹⁰ used to prepare their "Strophanthin." The seeds were extracted with hydrochloric acid containing alcohol (1 part HCl in 10 parts alcohol). The filtered extract was diluted with water and evaporated until strophanthin separated out. The filtered, well-washed sediment was recrystallized three times out of alcohol and gave pure white silky crystals, which proved to be identical with strophanthin, prepared from strophanthin.

Feist¹¹ did not prepare strophanthin himself. The strophanthin used by Feist for his investigations was prepared by Boehringer and Sons (Waldhof) from Kombe Strophanthus seed by Fraser's process,¹² also a preparation of Schuchardt out of hispidus seed was found to be identical with the former preparation.

Properties. Strophanthin forms a fine white powder with a crystalline structure, or a brittle mass when obtained by evaporating a watery solution. It does not contain nitrogen and does not reduce Fehling's solution in the cold or by heating. It contains water in varying amounts. One cannot say whether the water is that of absorption or of crystallization. Feist gives the result of only one estimation: dried at 110° 7.48% H₂O. For the results of combustion and other data, see table.

Strophanthin was hydrolized with five times its weight of half percent hydrochloric acid. The flask was placed in a cold waterbath, and slowly heated. At 30° it was all dissolved and at 70-75° strophanthin separated in small needles. After having kept the fluid some time at 75-80° it was cooled and filtered. The strophanthin washed with a little sulphuric ether forms a white crystalline powder. The filtrate from the strophanthin heated again at 75-80° separates out only a very small amount of the same product. Boiling the fluid gives very poor results, because resins are formed. Strophanthin contains two molecules of water of crystallization. By drying only one and one-half molecules can be driven off.

The water-free strophanthin was prepared by recrystallizing several times from methylalcohol. A crystalline substance was thus obtained, consisting of one molecule strophanthin and one molecule of methylalcohol. By drying this substance at 100° water-free strophanthin was obtained. Strophanthin hydrate melts at 169-170°, foaming at 176°, solidifying by cooling and melting again at 232°. The hydrate was examined optically and the crystals measured by Riva. The crystals are found to be monoclinic hemimorph. (See table).

By studying the action of alkalis on strophanthin Feist determined that strophanthin is a dilacton $\text{OHC}_{25}\text{H}_{37}\text{O}_2 \begin{matrix} \text{<CO-O>} \\ \text{<CO-O>} \end{matrix}$. By the action of alkali on strophanthin a salt of a dibasic acid is formed. By acidulating the solution of this salt and boiling, the original dilacton is not formed again, but *another lacton*, therefore, at least one OH is also present.

¹⁰Journal de Pharm., 1877, 25, p. 177, nearly the same in Comptes rendus 84, p. 261.

¹¹Berichte 31, p. 534, 33, p. 2063 and p. 2069 and p. 2091.

¹²See the preceding abstract concerning the examination of the seed by Prof. Hartwich.

The second cleavage of strophanthin, *strophantobiose methyl-ether*, was separated from the filtrate of strophanthidin. The combustion and the molecular weight estimation lead to the formula $C_{18}H_{24}O_{10}$. Strophantobiose-methylether was hydrolyzed by 1% sulphuric acid. In the fluid, resulting from this reaction, mannose was identified by the hydrazon and the osazon; rhamnose by the p-nitrophenyl rhamnosazon and by distilling the strophantobiosid with 30% sulphuric acid under which circumstances methylfurfurol is formed. Methylalcohol was identified by making a methoxyl estimation in strophantobiose-methylether. We are surprised that with the skill of Feist, the rhamnose was not obtained as a crystalline substance, as rhamnose crystallizes readily.

*Heffter and Sachs*¹⁸. Our investigations on the active principles of Kombe *Strophanthus* seed were already practically finished when the work of Heffter and Sachs appeared. Fortunately the publication of this paper was postponed so that we are able to incorporate the data of Heffter and Sachs. Their work is of especial importance to us as they studied the active principles of identified hispidus seed and unidentified Kombe seed, whereas we studied the active principles of identified Kombe seed and unidentified hispidus seed. The concordant results indicate that hispidus and Kombe seed, which are on the market are pure or that if they contain other species, these species do not contain other active principles.

Heffter and Sachs used for the preparation of strophanthin the method of Thoms (Berichte 31, p. 271). The fat free powdered identified *Strophanthus* Hispidus seeds were exhausted with hot 94% alcohol. The alcohol was distilled off and the residue taken up with hot water. To the slightly acid, colored, turbid solution lead acetate in excess was added. Hydrogensulphide was passed through the filtrate in order to remove the lead, calcium carbonate in excess was added to the clear and nearly colorless acid solution and evaporated on the waterbath to a thin syrup and filtered. The strophanthin was at last salted out by a large amount of ammonium sulphate, and the strophanthin obtained was further purified by repeated extraction with 94% alcohol and at last by precipitating from the absolute alcoholic solution with ether. In this way a yield of about 1.7% pure amorphous hispidus strophanthin was obtained. Kombe *Strophanthus* seed obtained in the open market gave 0.4-0.5% of crystalline Kombe strophanthin (which separated by evaporating the solution with calcium carbonate) and gave further an amorphous strophanthin, which was found to be apparently identical with amorphous hispidus strophanthin.

The figures of the analyses of these strophanthins obtained by Heffter and Sachs are compared in the table.

It is worth noting that Heffter and Sachs, using the modified method of Fromme (Hager's Handbuch der pharmac. Praxis Ergaenz band S. 669, 1908), for the quantitative strophanthidin determination, obtained values higher than ours, and probably nearer the theoretical.

OUR OWN RESEARCH.

Twenty-two Kg. *Strophanthus* Kombe seed in pods¹⁴ gave 8.2 Kgs. seed (37.3%), 8.1 Kg. pods (36.8%), and 4.7 Kg. comose hair¹⁵. Helbing¹⁶ who

¹⁸Biochemische Zeitschrift 40 (1912), p. 83.

separated five pods gives the average; seeds, 37.36% pods, 37.61%—hairs, 25.02%. The 8.1 Kgs. seed were ground to a coarse powder¹⁷ and extracted in a percolator with petroleum ether, to remove the fat. The yield was 5.6 Kg. fat free powder and 2.5 Kg. green fatty oil (30.9%). Fraser¹⁸ found 31.8% petroleum ether extract; 1.5 Kg. seed were twice percolated with 12 liters of 70% alcohol each time.¹⁹ The alcohol of the first percolation was distilled off in vacuo. The thin extract, after standing a few days deposited *crystals of strophanthin* which were suctioned off on a hardened filter. These crystals were recrystallized several times by dissolving in as little boiling water as possible and evaporating the solution at about 40°. By constant stirring at this temperature fine crystals were obtained, but the yield of crystalline strophanthin becomes smaller by every recrystallization., e. g., 5 gm. pure crystalline strophanthin was recrystallized in this way and gave only 2 gm. crystalline strophanthin and 3 gm. of a white amorphous substance. The amorphous substance is more readily soluble in water than the crystalline strophanthin.

While the crystalline strophanthin is *neutral*, the amorphous substance is in an aqueous solution *acid* in reaction. As will be shown later the estimation of the water of crystallization and the combustion of the crystalline strophanthin give figures, which agree with the calculated figures for the formula $C_{40}H_{56}O_{15} + 3H_2O$, while the estimations of the amorphous substance lead to the assumption that the amorphous substance is either a monobasic acid of the formula $C_{40}H_{56}O_{16} + 3H_2O$ resulting from the action of water on one lacton group $C_{39}H_{56}O_{13} \begin{matrix} \text{CO-O} \\ | \\ \text{O} \end{matrix} + H_2O = C_{39}H_{56}O_{13} \begin{matrix} \text{COOH} \\ | \\ \text{OH} \end{matrix}$ or a mixture of e. g. a monobasic acid, a dibasic acid and the original crystalline substance. It will be shown, that the strophanthidin, which results by the splitting of strophanthin with acids, is identical with Feist's strophanthidin, which he showed to be a dilacton. A study of the salts which amorphous acid strophanthin can form will doubtless have a bearing on the constitution of the amorphous acid strophanthin. The figures obtained by the combustion and titration of amorphous acid strophanthin will be compared with the calculated figures for the formula of monobasic acid strophanthin of the above given formula.

The reversion of the amorphous acid into the crystalline lacton could not be accomplished. It is interesting to note that the *figures obtained by the combustion of the amorphous body are the same as those obtained by Arnaud and by Kohn and Kulisch for their strophanthins.*

The following method of preparation, which is similar to the method of Arnaud

¹⁴This seed, as has been previously mentioned, was found by Prof. E. M. Holmes to be seed of *Strophanthus Kombe Oliv.*

¹⁵The comose hair was not gathered with the same care as seeds and pods, because the hairs contained no strophanthin, and the separating of the seeds being a rather disagreeable work, the dust affecting the mucous membrane of the nose, the separating was done in a well-ventilated room.

¹⁶The *Pharmaceutical Journal and Trans.*, 1887, 17, p. 748.

¹⁷It is easier, as we afterwards found, to pound the seeds and after one extraction with petroleum ether to grind the extracted mass to a fine powder and extract it again to remove all the fatty oil, for it is impossible to grind to a fine powder the seeds containing fats.

¹⁸The *Pharmaceutical Journal and Trans.*, 1889, 20, p. 329.

¹⁹Physiological testing, by Mr. O. E. Closson, showed that four successive extractions, made in the above-mentioned proportion, removed in the first percolation 86.5%, in the second percolation 9.4%, in the third percolation 2.4%, and in the fourth percolation 1.7% (considering 100% to be the whole amount of active substance extracted by these four percolations). Therefore, nearly all active substance is extracted in the first and second percolation.

(the recrystallization of the impure strophanthin being the only differences) was afterwards adopted, because the alcoholic extract did not always crystallize and Arnaud's method gives a better yield.

Crystalline strophanthin as we have shown can be obtained without any chemical purification from the alcoholic extract. It is thus possible to determine whether a certain chemical method of preparation of strophanthin from Strophanthus Kombe seed, gives a yield of naturally occurring crystalline strophanthin or of a derivative of strophanthin.

Method of preparation. 1.5 Kg. ground, fat free Strophanthus seed was percolated with 12 liters 70% alcohol and the percolate was distilled off in vacuo until about 1 liter fluid remained. To this fluid sufficient lead subacetate solution (Liquor plumbi subacetatis, U. S. P.) was added, to obtain an easily filtering mixture. The filtrate is a clear yellow fluid. The excess of lead was removed by hydrogen sulphide and the clear filtrate was evaporated at 40°-45° with constant stirring. Until the fluid becomes concentrated it is important that it be kept alcoholic by frequent addition of a little alcohol. When the fluid has become a thin extract, the alcohol must be evaporated as much as possible. It will then crystallize readily. The crystals are separated on a hardened filter of large surface by suction. The recrystallization is made in the following manner to avoid conversion into the amorphous body. The crystals are dissolved by placing them in a dish with a small amount of 94% alcohol and heating to 40-45° and stirring occasionally. After having filtered the solution, the alcohol is now evaporated to a thick extract at this temperature and water is added until a thin extract is obtained. With constant slow stirring with a motor, the extract is again evaporated to remove the rest of the alcohol. The extract will then crystallize readily. As was observed by Arnaud, the alcohol cannot be used alone to recrystallize, because it leaves strophanthin as a varnish. This recrystallization is repeated until strophanthin is obtained with the properties, which will be described.

Another method of preparation was carried out as proposed by Bourquelot and Herissey²⁰ to exclude enzym action, by adding 2.6 Kg. fat free ground seed to 15 liter boiling alcohol of 94%. After boiling for twenty minutes the hot fluid was filtered off and the alcohol evaporated in vacuo; this gave an extract from which crystalline strophanthin identical with the crystalline strophanthin made by the previously described method was obtained.

Crystalline strophanthin, identical with the former described crystalline strophanthin, was also obtained by the method, described, from Strophanthus Kombe seed, regularly purchased for the manufacture of Tr. of Strophanthus. The first crystalline strophanthin will be called: strophanthin (ident.), the second: strophanthin (trade). No difference was found between them.

Properties of crystalline strophanthin. Kombe strophanthin (ident. and trade) is a white crystalline substance, showing under the microscope fine needles or long plates.

It contains three molecules of water of crystallization, which are readily given off in a vacuum desiccator more quickly in vacuo at 80°. By placing the dehydrated crystals in a chamber containing moist air the water is taken up again. In

²⁰Comptes rendus, 133, p. 690.

a vacuum at 100° C. or 105-110° C. no more water is given off than in vacuo at 80° C. Found by drying at 80° C. and 105-110° C. in vacuo for Strophanthin (ident.): 6.0%-6.5%-6.3%. In strophanthin (trade) 7.1 and 7.0%. Calculated for $C_{40}H_{88}O_{18} + 3H_2O$: 6.5% H_2O .

Melting point. The substance melts in its water of crystallization at 158-165°C., becoming a turbid mass. Dried, it melts at 178-179° C. Strophanthin (trade)



Crystalline Kombé-strophanthin.

gave the same results, and by mixing them together the same results were obtained.

Specific rotation was determined in 94% alcoholic solution of air-dried substance.

I. 1.000 gm. cryst. strophanthin (ident.) dissolved in 25 cc. 94% alcohol.

$$\begin{aligned} \text{(a)} \quad D &= \frac{100\alpha}{lc} = +31.6 & l &= 2 \\ & & \alpha &= +2.53^\circ \end{aligned}$$

II. 0.7500 gm. cryst. strophanthin (ident.) dissolved in 25 cc. 94% alcohol.

$$\begin{aligned} \text{(a)} \quad D &= \frac{100\alpha}{lc} = +31.6 & l &= 2 \\ & & \alpha &= +1.90^\circ \end{aligned}$$

III. A determination was also made in absolute (99.5%) alcohol.

0.7500 gm. cryst. strophanthin (ident.) dissolved in 25 cc. 99.5% alcohol.²¹

$$\begin{aligned} \text{(a)} \quad D &= \frac{100\alpha}{lc} = +31.3 & l &= 2 \\ & & \alpha &= +1.88^\circ \end{aligned}$$

IV. A determination was also made in watery solution (to compare with Arnaud's value).

a. 0.200 gm. cryst. strophanthin (ident.) dissolved in 25 cc. water.

$$\begin{aligned} \text{(a)} \quad D &= \frac{100\alpha}{lc} = +28.7\% & l &= 2 \\ & & \alpha &= +0.23^\circ \end{aligned}$$

b. 0.7500 gm. cryst. strophanthin (trade) dissolved in 25 cc. 94% alcohol.

$$\begin{aligned} \text{(a)} \quad D &= \frac{100\alpha}{lc} = +30.5 & l &= 2 \\ & & \alpha &= +1.83 \end{aligned}$$

Combustion.

I. 0.2670 gm. cryst. strophanthin (ident.) dried at 80° in vacuo gave 0.1947 gm. H_2O and 0.6073 gm. CO_2 .

II. 0.2318 gm. cryst. strophanthin (ident.) dried at 105-110° in vacuo gave 0.1667 gm. H_2O and 0.5291 CO_2 .

²¹For differences in rotation of alkaloids in 94% alcohol and absolute alcohol. See Jour. of Chem. Society (London), 1910, 97, p. 1328.

III. 0.2875 gm. cryst. strophanthin (ident.) dried at 105-110° in vacuo gave 0.1846 gm. H₂O and 0.6047 gm. CO₂.

IV. 0.2520 gm. cryst. strophanthin (trade) dried at 105-110° in vacuo gave 0.1802 gm. H₂O and 0.5680 gm. CO₂.

V. 0.2597 gm. cryst. strophanthin (trade) dried at 105-110° in vacuo gave 0.1872 gm. H₂O and 0.5863 gm. CO₂, or in percent:

	S. Ident.			S. trade		Aver. S. ident.	Aver. S. trade	Calculat. f. C ₄₀ H ₅₈ O ₁₅
C	I	II	III	IV	V	61.97	61.52	61.32
H	82.03	82.25	81.65	81.47	81.57	7.98	8.04	7.27
	8.17	8.06	7.73	8.01	8.08			

An aqueous solution of cryst. strophanthin has the following properties: Heated with a small amount of a mineral acid and made alkaline afterwards, it readily reduces Fehling's solution.

Crystalline strophanthin can be boiled with glacial acetic acid without producing a substance capable of reducing Fehling's solution. A trace of crystalline strophanthin, when added to sulphuric acid first turns dark green and then brownish.²²

It gives a white precipitate with tannic acid solution and no precipitate with lead acetate or basic lead acetate solution.

Properties of amorphous acid strophanthin. Acid strophanthin was not obtained in a recognizably crystalline form. It is difficult to determine how much water is present as a hydrate, since amorphous acid strophanthin is hygroscopic. This water is readily given off in vacuo at 100° C., no more water being given off in vacuo at 105-110° C. Found by drying in vacuo at 105-110° 5.9%, in other samples 7.7% and 8.0% of water. Calculated for C₄₀H₅₈O₁₆+3H₂O 6.37%.

Melting point. Acid strophanthin softens at about 100° C. in its hydrate water and melts at 165-170° C. The dried substance softens at 160° C. and melts about 180° C.

Specific rotation was determined in watery solution of air-dry substance 0.400 gm. dissolved in 25 cc. water.

$$D = \frac{100\alpha}{lc} = +20.6 \quad l = 2 \quad \alpha = +0.33$$

Combustion.

I. 0.3375 gm. amorph. acid strophanthin (ident.) dried at 105-110° in vacuo gave 0.2333 gm. H₂O and 0.7477 gm. CO₂.

II. 0.2553 gm. amorph. acid strophanthin (ident.) dried at 105-110° in vacuo gave 0.1717 gm. H₂O and 0.5672 gm. CO₂.

III. 0.2316 gm. amorph. acid strophanthin (trade) dried at 105-110° in vacuo gave 0.1609 gm. H₂O and 0.5145 gm. CO₂.

IV. 0.2645 gm. amorph. acid strophanthin (trade) dried at 105-110° in vacuo gave 0.1873 gm. H₂O and 0.5899 gm. CO₂, or in percent:

	Ident.		Trade		Aver. trade	Aver. ident.	Calc. f. C ₄₀ H ₅₈ O ₁₆
C	I	II	III	IV	60.70	60.50	60.42
H	60.42	60.59	60.58	60.82	7.86	7.62	7.36
	7.75	7.50	7.79	7.94			

Molecular Weight of Crystallin Kombe Strophanthin and Other Kombe Strophanthins.

Feist (Berichte 31 (1898), p. 536 and 33 p. 2075), determined the molecular weight of Kombe strophanthin. In his first preliminary report Feist said: "The chosen formula (C₂H₃O)₁₆ is also supported by the cryoscopic molecular weight

²²Reaction of Helbing. The Pharmac. Jour., 1877, 17, p. 924.

determination in water. Calculated 688, found in the average 678 and 680. Notable molecular association occurs with increasing concentration."

The figures found by the determination are reported in his following paper in which Feist says: "The cryoscopic molecular weight determinations can only be determined in water ($c=18.9$) and give very uncertain results, calculated $C_{40}H_{86}O_{19}=850$.

I. Used air-dry strophanthin hydrate in tablets.

Substance.	Depression.	Mol. Weight Found.	Average Mol. Weight.
0.0956	0.030	572.8	678.5
0.2520	0.069	656.0	
0.3997	0.089	806.8	

The amount of water used was 10.52 gm.

II. Used strophanthin, which was dried several months over sulphuric acid, hygroscopic powder.

Substance.	Depression.	Mol. Weight Found.	Average Mol. Weight.
0.3155	0.079	614.1	680.8
0.6598	0.150	655.3	
1.2178	0.249	752.1	

The amount of water used was 12.29 gm.

The following are the figures obtained by our own research.

The strophanthins used for the experiments were:

I. Crystalline Kombe strophanthin, II, acid amorphous Kombe strophanthin (obtained by the action of water on crystalline Kombe strophanthin), III, amorphous strophanthin Merck.

Ia. Crystalline Kombe strophanthin.

Substance.	Depression.	Mol. Weight Found.	Calculated for $C_{40}H_{86}O_{19}$
0.0874	0.023	481	776
0.1785	0.037	611	

The amount of water used was 15.01 gm.

Another determination was made with crystalline Kombe strophanthin.

Ib. Crystalline Kombe strophanthin.

Substance.	Depression.	Mol. Weight Found.	Calculated for $C_{40}H_{86}O_{19}$
0.0517	0.012	551	776
0.1451	0.032	577	
0.2344	0.053	563	

The amount of water used was 14.91 gm.

II. Acid amorphous strophanthin.

Substance.	Depression.	Mol. Weight Found.	Calculated for $C_{40}H_{86}O_{19}$
0.1865	0.061	390	794
0.3940	0.100	503	
0.5223	0.139	486	

The amount of water used was 14.9 gm.

III. Amorphous Kombe strophanthin-Merck.

Substance.	Depression.	Mol. Weight Found.
0.1407	0.030	596
0.2740	0.054	645
0.4246	0.081	666

The amount of water used was 14.95 gm.

These figures are in agreement with those of Feist for the same concentration. The last determination of the first experiment of Feist is undoubtedly an error. From these figures we observe that with higher concentration the molecular weight increases, therefore the figures of Feist's second experiment become close to the theoretical (776). Feist's explanation of this behavior was that the uncertain results are due to notable molecular *association* by increasing concentration. Through our recent investigation of the conversion of crystalline Kombe strophanthin into the acid amorphous strophanthin we are able to give a better explanation, viz: *dissociation*. This is already indicated by the figures of Feist in which all his molecular weight determination fall well below the calculated.

The molecular weight was therefore determined in a non-ionizable fluid, which at the same time possesses sufficient solubility for strophanthin, in order to obtain the correct values. These fluids, alcohol, acetone, etc., could only be used conveniently by determining the increase in boiling point. The Beckman apparatus was used in which heating is accomplished by circulating vapor (Zeitschr. f. physik. Chemie, 40, 1902, P. 133).

The determination was made with alcohol as a solvent. Beckman determined the constant (molecular increase for 100 cc.)=15.6°.

Ia. Crystalline Kombe-strophanthin.

Cc. of alcohol.	Gm. Subst.	Observed increase	Gm. Subst. in 100 cc.	Found Mol. W.
14.1	0.3020	0.042	2.1464	797
15.7	0.3020	0.028	1.2850	716

Ib. Crystalline Kombe-strophanthin.

Cc. of alcohol.	Gm. Subst.	Observed increase	Gm. Subst. in 100 cc.	Found Mol. W.
12.7	0.3947	0.058	3.1080	836

The average molecular weight found for crystalline Kombe Strophanthin $1/3(797+716+836)=783$. Calculated for $C_{40}H_{56}O_{15}=776$.

II. Amorphous Kombe-strophanthin Merck.

Cc. of alcohol.	Gm. Subst.	Observed increase	Gm. Subst. in 100 cc.	Found Mol. W.
11.6	0.3116	0.044	2.6862	952
12.7	0.3116	0.037	2.4535	1034
14.4	0.3116	0.032	2.1639	1055

The average molecular weight found for Kombe strophanthin Merck $1/3(952+1034+1055)=1014$. The barometer stood constant during the experiments.

We believe that crystalline Kombe strophanthin contains two lacton groups, which may be different from the strophanthidin grouping, in that there are OH

radicals in the sugar which may interact with the formation of different lacton complexes and of internal ethers, thus accounting for the two less molecules of water in the molecule of strophanthin than would otherwise be expected. When dissolved in water both of these lacton groups hydrolyze to a certain extent into acids, which by their ionization give different molecular weight values, depending on the concentration. Therefore, by greater dilutions the apparent molecular weight calculated, according to the formula of Raoult is smaller, whereas by increasing concentration the molecular weight approaches the molecular weight of the calculated formula. For the acid amorphous strophanthin we believe that the molecule has undergone a rearrangement by which one of the lacton groups is converted permanently into an acid, which remains an acid independent of the concentration.

A simple reaction demonstrated that amorphous Kombe strophanthin Merck must contain a certain amount of acid amorphous strophanthin. Three pieces of blue or neutral litmus paper are moistened with water. A small amount of crystalline Kombe strophanthin is put on one, on the second a small amount of acid amorphous Kombe strophanthin, and on the third piece of litmus paper a small amount of amorphous Kombe strophanthin Merck. The papers indicate (by looking on the other side) that only crystalline Kombe strophanthin is neutral, whereas the other samples behave as acids.

Contrary to Feist's explanation, we find that the lower figures obtained with the cryoscopic molecular weight determination are due to a dissociation of the molecule.

By using alcohol with the ebullioscopic method nearly theoretical figures were obtained for the molecular weight of crystalline Kombe-strophanthin.

Titration of amorphous acid strophanthin with N/10 sodium hydroxide, phenolphthalein as an indicator.

I. 0.5000 gm. amorph. acid strophanthin (air dry) was dissolved cold in 10 cc. N/10 sodium hydroxide and titrated back with N/10 oxalic acid. Found: that 3.2 cc. N/10 sodium hydroxide was necessary to neutralize the strophanthin.

II. The same investigation repeated with 0.5000 gm. air-dry amorph. acid strophanthin gave as result that 3.1 cc. N/10 sodium hydroxide was necessary to neutralize the strophanthin.

III. 0.5000 gm. amorphous acid strophanthin (air dry) was dissolved in 10 cc. N/10 sodium hydroxide and heated until the fluid boiled. The cooled solution was titrated back with N/10 oxalic acid. Found: that 5.5 cc. N/10 sodium hydroxide was necessary to neutralize the strophanthin. Repeating the boiling with more alkali gave only a slight increase of the neutralizing value.

IV. The same investigation as III repeated with 0.5000 gm. air-dry amorph. acid strophanthin showed that 5.4 cc. N/10 sodium hydroxide was necessary to neutralize the strophanthin.

Found in the cold for 0.5000 gm. acid strophanthin: 3.2 cc. and 3.1 cc. N/10 NaOH.

Found by heating for 0.5000 gm. acid strophanthin: 5.5 cc. and 5.4 cc. N/10 NaOH.

Calculated for 0.5000 gm. monobasic strophanthin ($3\text{H}_2\text{O}$) 5.88 cc. N/10 NaOH.

Amorphous acid strophanthin is much more soluble in water than crystalline strophanthin. A watery solution of amorphous acid strophanthin has the following properties.

It slowly reduces Fehling's solution by boiling (a fresh aqueous solution of crystalline strophanthin dissolved in the cold does not reduce Fehling's solution by boiling).

Heated with a small amount of a mineral acid and made alkaline afterwards; it readily reduces Fehling's solution. It gives a white precipitate with tannic acid solution and no precipitate with lead acetate or basic lead acetate solution.

A trace of amorphous acid strophanthin, when added to sulphuric acid first turns greenish brown and then brown.

When a 12% solution of hydrochloric acid containing crystalline or amorphous strophanthin is boiled no appreciable amount of furfural or methylfurfural is formed.²³

0.2000 gm. pure rhamnose ($\text{C}_6\text{H}_{14}\text{O}_6$) was distilled with 500 cc. 12% hydrochloric acid from a round flask, which was connected with a condenser by a ground joint. The distilling fluid was gathered in an Erlenmeyer flask, which had a mark indicating 400 cc. A small piece of unglazed porcelain was added to the boiling fluid to prevent bumping. The round flask was heated in an air bath. After about 4 hours the distillation was ready and to the clear distillate a filtered solution of 0.300 gm. pure phloroglucin in about 15 cc. warm 12% HCl was added and the Erlenmeyer flask was kept dust free for 15-18 hours. Then the methylfurfural-phloroglucid, which had settled as a red precipitate, was filtered on a weighed quantitative filter, which had been dried at 97-100°. The precipitate was washed with 150 cc. water and the filter with precipitate dried for 3½-4 hours at 97-100° and weighed. 0.200 gm. rhamnose ($\text{C}_6\text{H}_{14}\text{O}_6$) gave 0.1310 gm. methylfurfural-phloroglucid or according to the formula of Ellett and Tollens. (Journal f. Landwirtschaft 1905, p. 13.)

Rhamnose = Ph. \times 1.65 — Ph² \times 1.84 + 0.010.

When Ph = amount of phloroglucid.

we find 0.209 gm. rhamnose.

The method was tried out on ouabain (gratus strophanthin), which according to Arnaud and also to Thoms has the formula $\text{C}_{30}\text{H}_{46}\text{O}_{12} + 9 \text{H}_2\text{O}$. Arnaud could separate crystalline rhamnose by splitting ouabain with acids. A quantitative estimation of rhamnose was made by Arnaud by titrating the fluids remaining by hydrolysis according to Soxhlet. Arnaud²⁴ found in this way 24.2% $\text{C}_6\text{H}_{14}\text{O}_6$ in $\text{C}_{30}\text{H}_{46}\text{O}_{12} + 9 \text{H}_2\text{O}$ calculated for 1 molecule $\text{C}_6\text{H}_{14}\text{O}_6$ 23.9%.

0.960 gm. air dry ouabain was distilled in the above described manner and gave 0.1540 gm. methylfurfuralphloroglucid or according to the formula of Ellett and Tollens found: 0.2205 gm. rhamnose in 0.960 gm. $\text{C}_{30}\text{H}_{46}\text{O}_{12} + 9 \text{H}_2\text{O}$ or 22.9%.

²³Concerning the furfural and methylfurfural estimations:

Krober—Jour. f. Landwirtschaft, 1900, p. 379.

Ellett and Tollens—Ber. 38, p. 492, Jour. f. Landw., 1905, p. 13.

Mayer and Tollens—Jour. f. Landw., 1907, p. 268, Ber. 40, p. 2441.

²⁴Comptes rendus 126 (1898), p. 1208.

The method was now applied to crystalline and acid amorphous strophanthin. 0.750 gm. air dry crystalline strophanthin gave 0.0074 gm. brownish phloroglucid. Calculating this as methylfurfurophloroglucid we get according to the formula of Ellett and Tollens 0.0211 gm. rhamnose ($C_6H_{14}O_6$) in 0.750 gm. air dry crystalline strophanthin or 2.9%. 0.850 gm. air dry amorphous acid strophanthin gave 0.0070 gm. brownish red phloroglucid. When we figure that it is methylfurfurophloroglucid, we get according to the formula of Ellett and Tollens 0.0215 gm. rhamnose ($C_6H_{14}O_6$) in 0.850 gm. amorphous strophanthin, or 2.5%. If air dry crystalline strophanthin ($C_{40}H_{58}O_{15} + 3 H_2O$) should contain 1 molecule rhamnose the percentage $C_6H_{14}O_6$ would be 21.9% and for the air dry amorphous acid strophanthin ($C_{40}H_{58}O_{16} + 3 H_2O$): 21.4%.

We can conclude, therefore, that *no rhamnose* is present in Kombe strophanthin.

According to Feist rhamnose and d-mannose should be present in Kombe strophanthin. If 2 molecules of d-mannose are contained in crystalline strophanthin then 0.750 gm. $C_{40}H_{58}O_{15} + 3 H_2O$ should contain 0.325 gm. mannose and 0.850 gm. $C_{40}H_{58}O_{16} + 3 H_2O$ should contain 0.359 gm. mannose. Therefore, 0.340 gm. d-mannose was distilled with 12% HCl to allow a comparison with the results of the former estimations. When 0.300 gm. phloroglucid was added to the distillate of 0.340 gm. mannose with 12% HCl *no precipitate* was visible after 18 hours. Therefore, d-mannose cannot be the reason of the formation of the small yield of phloroglucid from strophanthin.

Strophanthidin. The strophanthidin prepared by Kohn and Kulisch from their strophanthin is different from the strophanthidin prepared by Feist. By splitting crystalline strophanthin by the method of Kohn and Kulisch or by other methods or splitting amorphous acid *strophanthin with 1% H_2SO_4 , the same strophanthidin was always obtained and this strophanthidin proved to be identical with that described by Feist.*

Strophanthidin was prepared from crystalline strophanthin by the method of Kohn and Kulisch. (See the prescription of this method above.)

It separated out in yellow crystals, which after recrystallizing three times from hot alcohol and concentrating the solution, separated in fine, large, colorless crystals, which showed under the microscope the same form as the picture of strophanthidin given by Feist. The following procedure gives a better yield than the method of Kohn and Kulisch: To 100 cc. boiling 1% HCl 5 gm. crystalline strophanthin in fine powder was added. After dissolving the strophanthin the fluid was cooled and strophanthidin separated quickly in fine white crystals, which were filtered by suction and washed with water. After two crystallizations from hot alcohol nice large crystals can be obtained. Amorphous acid strophanthin separates a dark resin when heated with 2% HCl. The best method to split amorphous acid strophanthin was found to be boiling with 1% H_2SO_4 . 6 gm. amorphous acid strophanthin was boiled with a reflux for one-half hour with 50 cc. 1% H_2SO_4 . The yellow separation was repeatedly crystallized from hot alcohol and gave the same strophanthidin as prepared from crystalline strophanthin, therefore, by the action of sulphuric acid, the acid group goes over to a lacton group.

(To be continued.)

PRESCRIPTION FAKES AND HEALTH AND BEAUTY TALKS.*

One of the "features" of the modern metropolitan daily is the "Woman's Page," in which is given, for the education or delectation of feminine readers, reading matter that ranges from the useful to the inane. Naturally enough, we find the important subject of care of the health learnedly (?) discussed by the "Madames" or "Mademoiselles" who have charge of these departments. To the "patent medicine" advertiser who would deceive the reader by publishing his advertisement in "reading matter" style, space on these "Women's Pages" is a valuable asset. A form of deceptive advertisement that of late has become very popular with nostrum exploiters has previously been referred to in these columns as "prescription fakes." The advertisements are usually set as reading matter, and contain information regarding the treatment of some physical ailment by means of the drugs contained in an innocent looking formula; usually all the drugs but one are official, the exception being a "patent medicine" with a name not unlike the pharmacopœial preparations. A modification of the "prescription fake" type of advertisement forms the subject of this article."

Every week or so "Mrs. Mae Martyn's" fake department will appear in the paper, the initials of the "correspondents" and the wording of the "answers" varying, but the usual changes being rung on spurmax, crystos, almozoin, canthrox, quinola, parnotis, kardene and luxor.

Should the innocent reader go to the drug store and ask, say, for four ounces of spurmax, she is given the inevitable "original package," consisting of a tin box bearing a label with the name of the preparation, the method of using it and the various conditions for which the nostrum is recommended. There is also the statement, "Made by H. S. Peterson & Co., 95-97 Kinzie St., Chicago." The company putting out these medicinal agents is not a firm of pharmaceutical chemists, but, we understand, manufactures flavoring extracts and does business largely by means of women agents throughout the country.

Four of these deceptively advertised nostrums were analyzed in the Association's laboratory. The laboratory report follows:

ALMOZOIN.

Almozoin, as found on the market, is a pale pinkish-white powder, having a faint odor like benzaldehyd. Qualitative examination of almozoin demonstrated the presence of magnesium, sodium, tragacanth, a carbonate and a borate. Free boric acid, ammonium salts and sulphates were absent. Magnesium and the borate radicle were determined and the tragacanth was approximately estimated. From the results of the examination it would appear that the composition of almozoin is essentially as follows:

Tragacanth (gum tragacanth).....	40 percent
Sodium borate (borax).....	40 percent
Magnesium carbonate	20 percent

(Retail price of almozoin, one-half dollar; estimated cost of ingredients, three cents.)

*Kansas State Board of Health Bulletin.

CRYSTOS.

The specimen package of crystos which was purchased contained about one ounce and was a coarse, white odorless powder. Qualitative tests demonstrated the presence of chlorid, free boric acid, borate, sodium and traces of sulphate. Alkaloids, ammonium salts, carbonates, heavy metals and potassium were absent. Determinations of chlorid and of free and of combined boric acid were made, from which it would appear that the composition of crystos is about as follows:

Dried sodium borate (dried borax)	20 percent
Sodium chlorid (common salt)	20 percent
Boracic acid	60 percent

(Retail price of crystos, one-half dollar; estimated cost of ingredients, one cent.)

PARNOTIS.

Parnotis is a pale, cream-colored, fine powder, having an odor resembling cologne, which dissolves in water and forms a turbid solution, which becomes clear by filtration. Qualitative examination of the preparation demonstrated the presence of bicarbonate, sulphate, sodium and traces of chlorid and of iron. Quantitative determinations of the sulphate and of the bicarbonate were made, from the results of which it would appear that parnotis consists essentially of:

Impure anhydrous sodium sulphate	25 percent
Sodium bicarbonate	75 percent

(Retail price of parnotis, one-half dollar; estimated cost of ingredients, less than two cents.)

SPURMAX.

Spurmax is a pink, crystalline powder, highly perfumed. Qualitative tests demonstrated the presence of magnesium and of a sulphate. The absence of more than traces of chlorid, carbonate, organic compounds and heavy metals was shown by the usual tests. Quantitative determinations were made for magnesium, for sulphate and for water. Microscopic examination indicated that the coloring matter was very unevenly distributed throughout the preparation, some crystals being colorless, while others were very highly colored. Essentially, spurmax consists of:

Crystallized magnesium sulphate (Epsom salts)	100 percent
Perfume	Trace
Coloring matter	Trace

(Retail price of spurmax, one-half dollar; estimated cost of ingredients, one cent.)

NEW FORM OF AN OLD TRICK.

Spurmax, then, when subjected to the critical light of analysis and shorn of the hypothetical virtues with which "Mrs. Mae Martyn" invests it, proves to be Epsom salts colored pink and rendered highly odoriferous; the "flesh reducer that . . . should reduce your weight ten pounds in a few weeks" contains, apparently, nothing more marvelous than sulphate and carbonate of soda—and so it goes. The old, old trick of the charlatan, the quack and the nostrum exploiter is again in evidence. Give some well-known drug a fancy name, disguise it physically if possible, advertise it as possessing marvelous virtues and sell it at a price out of all proportion to its value.

"HEALTH AND BEAUTY TALKS."

For several months past many newspapers have been carrying on the "Woman's Page" what, to the uninitiated, appears to be a department devoted to answering queries regarding health. The "department" is entitled "Health and Beauty Talks," or "Health and Beauty Helps," or "Aids," or "Secrets"—the last word of the title varying with the copy. Under the title is the legend, "By Mrs. Mae Martyn." The subject matter consists of information(?) on questions of health, given in the "answers to correspondents" form; the first and last "answer" usually makes reference to none but simple home remedies or pharmacopœial preparations. For instance:

"Q. 1. A good foot wash is made of a pint of water, to which is added a tablespoonful of salt and a pinch of alum and a few drops of arnica."

Every other "answer," however, contains a "joker" in the form of nostrum which is referred to in such a way as to lead the unsuspecting reader to imagine that it is but an ordinary official drug. Thus, in the advertisement before us, there are nine replies. Here is a sample:

"Ethel J.: (1) It made me happy to read your letter. I am glad you think so well of my recipes that you cut them out and pass them along to your friends. None should have difficulty in getting from her druggist any ingredient I name, for I never advise use of anything that is not sold in first-class drug stores everywhere. (2) The only objection I know to the use of liquid complexion beautifiers is their high cost when purchased in a ready manufactured state. You can make at home a fine 'liquid powder' that softens and whitens the skin by putting two teaspoonfuls of glycerin and four ounces of spurmax in one-half pint of boiling water; let stand until cold. Apply with the palm of the hand and rub until dry. I prefer this spurmax wash to any face powder I can buy."

The "joker" in this answer," of course, is spurmax. In the other "replies," all worded in the same deceptive way, the reader is urged to get—

Crystos—"For tired and inflamed eyes."

Almozoin—"For blackheads, . . . freckles and tan."

Canthrox—"For shampooing purposes."

Quinola—"To remove dandruff, stop falling hair, relieve itching . . . and promote the growth of hair."

Parnotis—"A flesh reducer that . . . should reduce your weight ten pounds in a few weeks."

Kardene—"A splendid blood tonic and liver invigorator . . . for pimples, yellow blotches, sallow complexion, scrofula and all eruptions of the skin."

Luxor—"A very dear friend of mine cured a most obstinate case of eczema with this remedy."

 RECIPROCAL INTERSTATE REGISTRATION.

WM. MITTELBACH, PH. G., BOONVILLE, MO.

Requiring the practitioner of pharmacy to be a graduate from a school of pharmacy, in addition to passing a state board, is the hitch or stumbling block that makes general interstate registration practically impossible. In those states where this is required by law, the non-graduate cannot possibly register, no matter