DEOLEATED TINCTURE OF STROPHANTHUS.

R. C. HOLMES, PH. C., PHAR. D., BROOKLYN, N. Y.

The U. S. P. Tincture of Strophanthus has long been a source of trouble to the pharmacist and manufacturer, inasmuch as the fixed oil, contained in the Kombe seeds, persists in clouding the preparation after standing a short time, or immediately upon chilling. Considerable difficulty is experienced before the tincture is fit for dispensing, repeated filtration being necessary in order to produce a clear tincture; this operation being necessary each time before filling a prescription.

The clinician's principal objections to the Tincture of Strophanthus are, that its nauseating properties, although less than those of the tincture of digitalis, produce untoward effects, and that oftentimes the preparation fails to give results.

Before the introduction of biological assay, the tincture varied from 40 to 400 percent; it can readily be seen at what point the source of unreliability lies.

Shoemaker[1] says: "With wider and more rapid dissemination of knowledge, we may hope that within a comparatively few years, we may have Strophanthus used as carefully as digitalis today." The modern methods of physiological standardization make it possible for Dr. Shoemaker's hope to become realized. The tincture of strophanthus, when standardized by modern biological assay, is an absolutely reliable preparation, which does not deteriorate. The pharmacist may replenish his stock and fill his prescriptions with a tincture invariably 100 percent active.

Therefore, we have the unreliability of Tincture of Strophanthus overcome by the introduction of biological assay. Now, if it is possible to do away with the nauseating and irritating properties, we have a preparation most desirable. Suspicion points to the fixed oil, the troublesome element, which makes the U. S. P. tincture an unsightly preparation and causes the pharmacist much inconvenience. Although it has been proven that the active principles possess certain irritating properties, it has been my purpose to prove that the fixed oil is a disturbing factor of considerable note. With this purpose in view, a series of experiments were carried out in this laboratory.

First. A U. S. P. tincture was prepared, the first percolate of about 800 cc. produced a clear alcoholic liquid, the percolate then clouded, and remained turbid in spite of repeated filtration. When the tincture was tested physiologically, it proved to possess a relative strength of 60 percent. (This particular shipment chancing to be an inferior grade of drug.)

Second. A 10 percent tincture was prepared after first completely extracting the fixed oil with pretroleum ether and percolating the deoleated drug with the U. S. P. alcoholic menstruum. A crystal clear tincture resulted, which remained clear after standing several weeks and after cooling to 0° C. The tincture, when tested physiologically, possessed a relative activity of 60 percent, proving that no loss in strength was suffered by the process of benzin extraction. Several

[1] Materia Medica and Therapeutics.

duplicate experiments were carried out, each of which checked the above results precisely.

The oil extracted from the seed was dark brownish green in color and amounted to 34 percent of the drug.

It possessed the following constants:

Sp. gr. at 25° C.	0.9018
Acid number	19.44
Sapon. number	187.52
Iodine number	95.63

Chemically pure petroleum ether was used in the extraction of the oil, thereby eliminating a possible chance of error due to dissolved impurities.

The National Standard Dispensatory assigns the following constants to the oil:

Sp. gr. at 25° C.	0.9249
Acid number	24.3
Sapon. number	194.6
Iodine number	101.6

No reference to the pharmacological action of the oil could be found.

The pharmacological properties of the oil were investigated, with the following results:

Twenty minims of the oil injected subcutaneously in a dog 5 kgm. in weight, produced no effect other than marked local irritation, which was very severe, the effect passing off after two hours.

Thirty minims of the oil, injected subcutaneously, produced severe local irritation.

Twenty minims of the oil were administered per os to a dog 5 kgm. in weight. The animal became very uneasy after 10 minutes, and was readily excitable. Judging from the behavior of the animal, there was severe pain in the region of the abdomen. The animal completely recovered from the effects after one hour.

Thirty minims of the oil were administered per os to a dog 5 kgm. in weight. The stage of uneasiness and excitability followed by emesis, which was very pronounced, and occurred one-half hour after injection. The animal then showed signs of depression, and fully recovered after three hours. The experiment was repeated several times, using several dogs while food was present in the stomach, and while the stomach was empty; always with the same results.

Smaller doses of the oil were given, varying from 5 to 15 minims, and invariably produced symptoms of gastro-intestinal disturbances varying with the amount of the dose. Vomiting, however, is not produced with doses smaller than 30 minims in a small dog.

It was deemed advisable to supplement the experiments by clinical observation, before arriving at conclusions. The tinctures (U. S. P. and deoleated), were concentrated to bring the preparation up to the standard adopted by this firm, and were then mailed to several physicians with instructions regarding the purpose of the experiment, etc. The tinctures were given, alternating, to patients taking the tincture regularly, and in all cases the deoleated tincture was preferred by the patient. The doctors reporting that the deoleated tincture undoubtedly possessed less irritating properties, and in every way was a more desirable

preparation. It is, therefore, hoped that the deoleated tincture of strophanthus will be made an official preparation to replace the tincture of the U. S. P. VIII.

In the estimation of the author, tincture of strophanthus is to be preferred to the tincture of digitalis, which is generally supposed to undergo rapid deterioration. This belief, however, was strongly disputed by Hatcher & Eggleston[2], but there are many facts yet to be established before such a radical view can be accepted.

LABORATORY OF PHARMACOLOGY AND EXPERIMENTAL MEDICINE, BRISTOL-MYERS CO., Brooklyn, N. Y.

ON CRYSTALLINE KOMBE'-STROPHANTHIN.

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

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Properties of strophanthidin. Under the magnifying glass strophanthidin shows the same shape of crystals as shown in the picture of strophanthidin given by Feist. It contains one molecule of water of crystallization. Feist had trouble in drying the substance and it was only by obtaining crystals of a methyl alcohol containing strophanthidin, which gave off readily the methyl alcohol at 100° C. that he could establish the formula for dry strophanthidin. Feist, and also Heffter and Sachs, did not dry in a heated vacuum, but only at ordinary pressure. By drying in vacuo at 110-115°, we could readily obtain crystalline water-free strophanthidin. Also at lower temperature (105° in vacuo) the water is given off, but slowly. In moist air the water is taken up again. Found: 3.56%, 3.50% and 3.02% calculated for $C_{27}H_{38}O_7 + H_2O$: 3.66% H_2O.

Melting point. Strophanthidin melts at about 120°C in its water of crystallization to a turbid mass and melts at about 170°C. The dried substance melts as Feist describes at 169°-170°C, foaming at 180°C, it becomes solid by cooling and then melts at 232°.

Specific rotation. 1.008 gm. air dry strophanthidin (from crystalline strophanthin) was dissolved in 25 cc. methyl alcohol.

$$(\alpha)_D = \frac{100\alpha}{lc} = +44.26 \qquad l = 2 \qquad \alpha = +3.57°$$

0.3300 gm. air dry strophanthidin (from amorph. acid strophanthin) was dissolved in 25 cc. methylalcohol.

$$(\alpha)_D = \frac{100\alpha}{lc} = +44.26 \qquad l = 2 \qquad \alpha = +1.17°$$

Feist found for 0.5043 gm. strophanthidin dissolved in 25 cc. methyl alcohol

$$(\alpha)_D = +45.45$$

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[2] Paper read before April meeting New York Branch of A. Ph. A.