

succeeded; and therefore will conclude with a quotation from an ancient sage.

Rabbi Tarfon: "Tis not incumbent on thee to complete the work;
Yet art thou not absolved from doing what thou canst."

(*Ethics of the Fathers, II, 21*)

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CAUSES OF DETERIORATION OF STROPHANTHUS SEED DURING STORAGE.*

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Experimental work being done in these laboratories on tincture of strophanthus brought out the information that a sample of *Strophanthus Kombé* seed which had originally assayed 120 to 133% U. S. P. deteriorated to such an extent during grinding and storage that at the end of one year it assayed only 37½ to 48½ U. S. P. strength. Since this deterioration was unexpected and unusual in our experience, a thorough search of the literature was made for the purpose of deter-

* Scientific Section A. Ph. A., St. Louis meeting, 1927.

mining, in this manner if possible, the conditions which favor and which inhibit such deterioration.

Tincture of *Strophanthus* is generally considered to be a very stable preparation. The deterioration of the seed was noted by Baldoni (1) who obtained a beautiful green coloration on treatment of the fresh seed with concentrated sulphuric acid, but less coloration when seeds which had been kept for a long time were similarly treated. Very little experimental work has been done on the factors determining the stability of *strophanthus* seed. In the absence of experimental work on this deterioration, a number of causes suggested by published material are listed below.

I. Effect of Light.—In 1911, Danielopolu (2) found that from an exposure, varying from thirty minutes to two and one-half hours, of *strophanthin* to ultra-violet rays its toxicity was very much lessened. Baldoni (1) has also reported that if light is allowed to act upon the seeds or the sun to shine upon them, the color reaction produced by concentrated sulphuric acid, which is supposed to be indicative of their activity, is weakened. This destruction of the active principle is more noticeable in the embryo than in the endosperm. The latter fact may be of importance in relation to the localization in the embryo of a hydrolyzing enzyme which will be discussed later.

II. Effect of Moisture and Heat.—It is well known that both crystalline and amorphous *strophanthin Kombé* are hydrolyzed by the action of acid solution and heat into the less active *strophanthidin*. Brauns and Clossen (3) have reported that by the action of heat on an aqueous solution of crystalline *strophanthin Kombé*, it undergoes in the absence of acid a change into an amorphous acid *strophanthin* which has only one-third the activity of the former. Boiling of the solution for fifteen minutes caused a loss of 15% of the activity. They state that a similar, though much slower, change is to be expected in the cold. It is therefore probable that the conditions of moisture under which the crude drug is stored will have considerable bearing on the reduction of the *strophanthin* content.

III. Effect of Molds.—Brauns and Clossen (3) have also reported that a 1:2000 aqueous solution of crystalline *strophanthin Kombé* kept for two weeks at room temperature showed the growth of mold and the loss of 50% of its activity. The extent to which the crude ground seed is protected from inoculation with molds and from conditions favorable for their growth during storage is therefore of probable importance.

IV. Effect of Enzymes.—It has been reported that the decreased toxic effect of *strophanthin Kombé* when given orally is due to the action of the digestive enzymes. Holste (4) found that it is only slightly decreased by a three and one-half hour exposure to pancreatin. It has recently been contended that the destruction of *strophanthin Kombé* in the digestive tract is due not to the presence of enzymes but to the presence of hydrogen ions in the gastric juice (5).

It has, however, been definitely shown that certain vegetable enzymes are capable of decomposing *strophanthin*. Miyadera (6) found that by previous mixture of spinach secretin with *strophanthin* the occurrence of the systolic heart cessation following administration was very definitely postponed. He ascribes this to an antitoxic action of the secretion on *strophanthin*. It seems probable that the results were caused by destruction of the *strophanthin* by enzymatic action

of the secretion. Tocco-Tocco (7) isolated from the cortex and embryo of strophanthus seeds, a substance which after 24 hours action on strophanthin at 30° caused the loss of the green color reaction with sulphuric acid. This substance was destroyed by heating the seeds at 100° for one-half hour. It was not present in the endosperm of the seed. Jacobs and Hoffman (8) have obtained from *Strophanthus Courmontii*, *Strophanthus eminii* and from *Strophanthus Kombé* seeds an enzyme which they have named strophanthobiase. This enzyme is capable of hydrolyzing *K*-strophanthin into cymarins and *d*-glucose, to the extent of 79% in 42 hours, 82% in 50 hours and 88% in 66 hours. From this work it seems probable that under certain conditions of storage the strophanthobiase which is present in the cortex and embryo of *Strophanthus Kombé* might cause considerable destruction of the strophanthin content of the seeds.

V. *Effect of Acids*.—As was stated above under the *Effect of Enzymes*, the hydrogen ions are capable of hydrolyzing both crystalline and amorphous strophanthin *Kombé* chiefly into strophanthidin which has only one-tenth the toxicity of the original strophanthin (3). All of the mineral acids and many of the organic acids, with the exception of carbon dioxide, hydrolyze strophanthin even in the cold (9, 10). Hydrolysis of the strophanthin content of the crude drug may result from the action of organic acids liberated by the decomposition of the organic matter of the seeds.

This material covers all the suggestions made in the literature as to the deterioration of strophanthin under conditions such as might occur in the storage of the crude drug, and all the information which was found on the deterioration of strophanthus seeds. The crude drug should therefore be protected from light, moisture, heat, and so far as possible from inoculation with mold spores.

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