

Oxime.—An attempt to prepare an oxime according to the technique of Vavon and Anziani (2) failed.

Color Reactions.—Celastrol and methyl celastrol gave a green color with ferric chloride. Acetyl celastrol, acetyl methyl and methyl acetyl celastrols gave no color with ferric chloride.

SUMMARY.

The bark of the root of *Celastrus scandens* contains no β -carotene. A red pigment has been isolated and named celastrol. Some of its physical properties and also those of some of its derivatives have been reported.

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NATURAL AND ARTIFICIAL CALAMINES FROM THE PHARMACEUTICAL, CHEMICAL AND PHARMACOLOGICAL STANDPOINTS.*¹

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INTRODUCTION.

The investigation of calamines began in 1803 when James Smithson (1) first distinguished chemically the differences between the silicate and the carbonate of zinc. Since then calamines have presented a challenging problem to pharmacists.

Prepared calamine N. F. VI is 98 per cent zinc oxide colored pink by the addition of a small amount of ferric oxide. It is extensively used for skin affections in the form of lotions and ointments. The question has been raised as to its merits over those of zinc oxide, and also whether the native calamine, generally described as impure zinc carbonate, and also precipitated zinc carbonate might not be better than the oxides.

This study was begun with the view of settling some of these questions.

HISTORY AND NOMENCLATURE.

There has been considerable confusion in the names applied to calamine. In the early history the oxide, carbonate and silicate of zinc were all known by the term cadmia or cadmea (4). At the present time, a native carbonate of zinc is called calamine by British mineralogists and smithsonite by Americans. The silicate of zinc is termed hemimorphite or electric calamine by the British, and calamine by the American mineralogists. In pharmacy, however, only the zinc carbonate has ever been recognized as calamine in both America and England.

The distinction between the silicate and carbonate of zinc by Smithson (1) in 1803 and the later work of Beudant (3) stimulated much interest in the commercial calamines. Following the work of Brett in 1837 many British and American workers turned to the analysis of them (6). The results in most cases showed that what appeared on the market as native zinc carbonate was barium sulfate colored with iron oxide. This situation was true in the British Isles, on the Con-

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tinant and in America. Even as late as 1909 and 1910 reports indicate that barium sulfate was still often sold for calamine. About this time interest in the composition of calamines waned and effort was directed toward the improvement of the preparations of calamine and an increased knowledge of its mineralogy.

CALAMINE, ITS PREPARATION AND USE.

Natural calamine has been largely replaced by prepared calamine which is made by adding the proper amount of jeweler's rouge to a suspension of zinc oxide. When the color is evenly suspended, the water is evaporated, and the paste properly dried and reduced to a fine powder. A second method for making prepared calamine is to roast zinc carbonate with the proper amount of ferric chloride (10). Lotions and liniments of prepared calamine have come into vogue in the twentieth century.

The estimations of the therapeutic values of calamine have not changed greatly since the Roman period. It was then used in the treatment of ulcers and diseases of the eyes, being recognized as a drying and healing agent. For almost two thousand years the therapeutic virtues which Pliny and Dioscorides ascribed to calamine have been accepted.

To-day, although calamine is colored zinc oxide and not native zinc carbonate, it is still recognized as a soothing and protective agent in skin conditions such as eczema and sunburn. It is also used, to some extent, in ambulatory cases of ulcers as a protective agent for newly forming skin.

OFFICIAL PREPARATIONS.

The United States Pharmacopœias from 1820 to 1850 included monographs on the native carbonate of zinc. In the Pharmacopœia of 1850 precipitated zinc carbonate appeared for the first time. In the 1860 revision the precipitated zinc carbonate was retained and the native carbonate deleted. In the revisions from 1870 to 1910 the precipitated zinc carbonate was retained in the Pharmacopœia. It was, however, deleted from the 1920 revision.

The National Formulary IV included a monograph which made the native zinc carbonate and calcined zinc carbonate, with a small amount of ferric oxide, official permitting a choice. Thus the native zinc carbonate was official again after sixty years. The fifth edition of the National Formulary retained only the prepared calamine which was described as zinc oxide containing small amounts of ferric oxide and silica. The National Formulary VI has retained prepared calamine as zinc oxide, not less than 98% ZnO, with a small amount of ferric oxide.

EXPERIMENTAL.

The native calamine (smithsonite) used throughout this study was obtained from China through the courtesy of Dr. B. E. Read of the Lester Institute, Shanghai. The sample was received in the form of small lumps with loose powder adhering. It was flesh to salmon in color, appearing darker after being pulverized. It was found not to be radioactive. By means of a mortar and a pebble mill the lot was reduced to a powder and passed through a 200-mesh sieve. Throughout the experimental work it has been designated as Chinese calamine. The official prepared calamine has been studied along with the Chinese product.

CHEMISTRY OF CALAMINES.

Prepared Calamine N. F. VI and Chinese Calamine were subjected to qualitative and quantitative analysis. The results are given in Table I.

TABLE I.

	Analysis.	
	Qualitative.	Quantitative.
Prepared Calamine N. F. VI	Iron, zinc carbonate, oxide	Zinc oxide 98.87%*
Chinese Calamine (Smithsonite)	Iron, zinc, calcium, mag- nesium (trace) Aluminum, carbonate, oxide, insoluble resi- due (trace)	Zinc† 14.79% repre- senting 18.43% zinc oxide

* The average of 2 assays.

† The average of 3 assays.

PRECIPITATED ZINC CARBONATE.

It was suggested that the antiseptic properties of precipitated zinc carbonate should be compared to those of calamine. It was prepared according to the directions of the U. S. P. V.

A semi-colloidal zinc carbonate was also prepared as follows: 100 ml. of 2.5 per cent sodium carbonate solution were added at the rate of 60 drops per minute to a solution of zinc sulfate, 6 Gm. in 200 ml. of a 2 per cent gelatin solution, with constant stirring. The precipitate was washed until free of sulfates. The particles assayed 1 to 1.5 microns in diameter.

BACTERIOLOGICAL TESTS.

A comparative study of the bacteriostatic property of the following compounds was made: prepared calamine N. F. VI, zinc oxide U. S. P. XI, zinc carbonate (A. R.), Chinese calamine, precipitated zinc carbonate and colloidal zinc carbonate. Each of these was incorporated in three different ointment bases and tested by the agar plate method using *Staphylococcus aureus* var. St. Louis and *Eberthella typhi* var. Rawlins as the test organisms.

Standard methods of testing were used and repeated sufficiently often to warrant reasonable conclusions as to results. No bacteriostatic action could be demonstrated for the six preparations named above. The variations in the bases employed had no effect on our results. The official ointment of ammoniated mercury was used as the control and gave uniformly positive results in every case.

A further attempt was made to test the bacteriostatic property prepared calamine N. F. VI, Chinese calamine, zinc oxide U. S. P. XI and zinc carbonate A. R. The agar cup plate method was used and *Eberthella typhi* var. Rawlins was the organism. A cup was made in the plate in the usual way and into it there was poured 1 Gm. of the powder suspended in water. The plates were incubated at 37° for 48 hours. The results were all negative.

It should be stated that this account is a brief summary of the results which are shown in several tables in the thesis. Inasmuch as the results are all negative, the tables are not being published.

A PROPOSED FORMULA FOR CALAMINE OINTMENT.

Objections have been made to the present official Ointment of Calamine, first because the directions for preparing it are not very specific and do not give a very smooth product. Second and perhaps more important, is the color. Because of the presence of yellow wax, lanolin and petrolatum the finished ointment has an unattractive color instead of an attractive pink which is obtained when white wax and white petrolatum are used. From a number of formulas which we have tried the following is suggested for consideration and study.

Prepared Calamine	17 Gm.
Liquid petrolatum or glycerin	11 Gm.
White wax	4 Gm.
Wool fat	4 Gm.
White petrolatum	64 Gm.

Procedure: Levigate the calamine with the liquid petrolatum or glycerin to a smooth paste. Melt the white wax, wool fat and the white petrolatum on a water-bath, remove and stir gently while cooling. Next add the cooled base, in divided portions, to the calamine and mix thoroughly to produce a smooth homogeneous ointment.

This ointment is easily prepared, has a good color, and spreads well when applied.

CLINICAL OBSERVATIONS.

The physicians of the Student Health Service, Purdue University, kindly coöperated in this study by using lotions of zinc oxide U. S. P. XI, prepared calamine N. F. VI, and Chinese calamine. The products were studied in part by being applied unilaterally to a symmetrical dermatitis. In some cases the lotions were applied and the results noted.

In all cases the patients reported that the applications were soothing. Such skin conditions as ringworm, drug dermatitis, dermatitis milia, soap dermatitis, dermatitis due to allergy and several unclassified cases of dermatitis were treated.

The physicians concluded that they could see no noticeable differences in the therapeutic action of these various lotions.

SUMMARY AND CONCLUSIONS.

1. Native American calamine is not available on the market. The samples which were obtained were silicates and not carbonate of zinc.
2. Several of the impurities which were reported as having been found in English calamine were also present in the Chinese calamine, namely, calcium, magnesium, iron and aluminum.
3. When tested in the form of ointments and suspensions by acceptable procedures, prepared calamine N. F. VI, zinc oxide U. S. P. XI, zinc carbonate A. R., Chinese calamine, precipitated zinc carbonate and semi-colloidal zinc carbonate were not bacteriostatic.
4. Clinical observations were made upon lotions of Chinese calamine, zinc oxide U. S. P. XI and prepared calamine N. F. VI and no differences as to their therapeutic action could be observed.

RECOMMENDATIONS.

1. In view of the fact that native American calamine is no longer available, and in view of the fact that native calamines, both foreign and domestic, are of uncertain composition and quality and furthermore that their superiority over prepared calamine as therapeutic agents has not been established, we recommend that prepared calamine be retained as an official product.
2. In view of the fact that the color of prepared calamine seems to have contributed to its acceptance as a medicinal agent, we recommend that the present formula for calamine ointment be changed so as to improve its color unless it can be shown that its therapeutic value is impaired by such a change.

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THE HOSPITAL DRUG BUYER.*

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Those who have any conception of the task involved in regulating the purchase and distribution of drugs and medicines for use in a hospital, regardless of its size, realize the many angles and the various needs that must be catered to, whether they be general or specific.

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