

Standard: The effects produced by a standard blistering ointment of the same formula as the ointment undergoing test and which has been proven to possess excellent blistering power by repeated practical physiologic tests as described above.

A typical physiological report on a satisfactory blistering ointment is herewith reproduced as a matter of interest:

VETERINARY BLISTERING OINTMENT—LABORATORY NO. —

*Effects.*

Horse No. 1.	Horse No. 2.	Horse No. 3.
A—Slight swelling	A—Slight swelling	A—Slight swelling
B—Small vesicles	B—Exudate	B—Vesicles
C—Sensitive	C—Sensitive	C—Sensitive
D—No hair removed	D—Practically no hair removed	D—No hair removed

Conclusions: A satisfactory blistering ointment.

SUMMARY.

Chemical analysis alone is not satisfactory as a means of standardizing blistering ointments, because the effect of the total amount of active ingredients is not exerted, owing to the limitations surrounding the employment of a product requiring contact in its use.

The standardization can be accomplished by chemical and physical control of manufacture of the ointments, coupled with physiologic tests on the finished product.

Detailed methods of chemical and physical control of manufacture and of physiologic tests on the finished products are described.

I am indebted to Dr. H. K. Wright of the Biological Laboratories of the H. K. Mulford Company, at Glenolden, Pa., for the details of the physiologic method outlined above.

PHARMACEUTICAL LABORATORIES,  
H. K. MULFORD COMPANY,  
PHILADELPHIA, PA.

CHINESE CANTHARIDES (*Mylabris Cichorii*). A WORTHY CANDIDATE  
FOR ADMISSION TO THE U. S. P.<sup>1</sup>

BY GEORGE E. ÉWE.

Previous to the World War, the Russian and Spanish Cantharides of the U. S. P. were practically exclusively employed in medicine. One of the minor effects of the war was to cut short supplies of U. S. P. Cantharides, so that recourse had to be made to the use of Chinese Cantharides, which was readily available, and which was vaguely believed to approximate in activity the official Cantharides.

This forced use of Chinese Cantharides has resulted in the accumulation of a sufficient amount of evidence to warrant the statement composing the title of this communication.

This evidence embraces the following attributes of this material: External use, internal use, cantharidin content, pharmaceutical behavior, price, and availability.

<sup>1</sup> Credit is due Dr. H. K. Wright of the Biological Laboratory of the H. K. Mulford Company at Glenolden, Pa., for conducting the physiological tests on veterinary blistering ointments, mentioned in this communication.

## EXTERNAL USE.

Cantharides is used externally for its rubefacient and blistering action, and for this purpose is usually prepared in ointment form.

Numerous physiological experiments conducted at the Biological Laboratories of the H. K. Mulford Company, Glenolden, Pa., have conclusively proven that weight for weight the activity of Chinese Cantharides is equivalent to Cantharides of the U. S. P.

In carrying out the experiments, the U. S. P. and Chinese Cantharides were converted into ointment form, all of the ingredients and the quantities of ingredients of the ointment being exactly the same, except for the use of U. S. P. Cantharides in the one case and the Chinese variety in the other.

The manner of conducting the comparative physiological experiments is indicated in a separate communication to this JOURNAL.<sup>2</sup>

In general, the process consisted of applying the ointment to a clipped area of the skin of a horse, following, in general, the conditions commonly employed in the practical use of veterinary blistering ointments, and noting and recording the following effects:

- A—Amount of swelling.
- B—Amount of exudation.
- C—Sensitiveness of the area.
- D—Whether the hair falls out or not.

At least two or three tests on different horses were made in order to eliminate the variation due to the varying thickness of skin of different horses.

This method of testing the activity of blistering ointments made with U. S. P. Cantharides has been in use for a considerable length of time by the company with which I am connected, and numerous lots of these ointments made with U. S. P. Cantharides had been tested and passed as satisfactory, previous to the necessity arising for the use of the Chinese variety. These numerous tests established a standard of activity for blistering ointments, which acted as a basis for comparison when it became temporarily necessary to employ Chinese Cantharides.

A few typical reports of physiologic tests on blistering ointments made with Spanish Cantharides of U. S. P. are given here as a matter of record and interest:

## BLISTERING OINTMENTS MADE WITH SPANISH CANTHARIDES.

*Ointment No. 1.**Effects.*

Horse No. 1.	Horse No. 2.	Horse No. 3.
A—Slight swelling	A—Slight swelling	A—Considerable swelling
B—Vesicles	B—Small vesicles	B—Large number of vesicles
C—Sensitive	C—Sensitive	C—Sensitive
D—Hair did not fall out	D—Hair did not fall out	D—Large quantity of hair came out

Conclusion: A satisfactory blistering ointment.

Horse No. 2 possessed a very thick hide. Cantharides used in this ointment assayed 0.967 per. cent cantharidin by the U. S. P. method.

<sup>2</sup> Preceding paper: "The Standardization of Veterinary Blistering Ointments," by George E. Éwe.

*Ointment No. 2.**Effects.*

Horse No. 1.	Horse No. 2.	Horse No. 3.
A—Slight swelling	A—Slight swelling	A—Slight swelling
B—Vesicles	B—Vesicles	B—Large amount of exudation
C—Sensitive	C—Sensitive	C—Sensitive
D—Some hair came out	D—A little hair came out	D—Some hair came out

Conclusion: A satisfactory blistering ointment. The cantharides used in this ointment assayed 0.645 percent cantharidin.

*Ointment No. 3.**Effects.*

Horse No. 1.	Horse No. 2.	Horse No. 3.
A—Slight swelling	A—A little swelling	A—Slight swelling
B—Small vesicles	B—Large exudate	B—Small vesicles
C—Sensitive	C—Sensitive	C—Sensitive
D—No hair removed	D—A little hair came out	D—No hair removed

Conclusions: A satisfactory blistering ointment. The cantharides used in this ointment assayed 0.685 percent cantharidin.

A few typical reports of physiologic tests on blistering ointments made with Chinese cantharides are also given here as a matter of record and interest, and also for a comparison of the effects with the effects yielded by the ointments made with the cantharides of the U. S. P.

## BLISTERING OINTMENTS MADE WITH CHINESE CANTHARIDES.

*Ointment No. 1.**Effects.*

Horse No. 1.	Horse No. 2.	Horse No. 3.
A—Slight swelling	A—Slight swelling	A—Slight swelling
B—Small vesicles	B—Exudate	B—Vesicles
C—Sensitive	C—Sensitive	C—Sensitive
D—No hair removed	D—Practically no hair removed	D—No hair removed

Conclusions: A satisfactory blistering ointment. The cantharides used in this ointment assayed 0.834 percent cantharidin by U. S. P. method.

*Ointment No. 2.**Effects.*

Horse No. 1.	Horse No. 2.	Horse No. 3.
A—Considerable swelling	A—Considerable swelling	A—Considerable swelling
B—Copious exudate	B—Copious exudate	B—Copious exudate
C—Sensitive	C—Sensitive	C—Sensitive
D—Some hair removed	D—Some hair removed	D—Some hair removed

Conclusions: A very active blistering ointment. No permanent scar resulted. The cantharides used in this ointment assayed 0.965 percent cantharidin.

*Ointment No. 3.**Effects.*

Horse No. 1.	Horse No. 2.
A—Slight swelling	A—Slight swelling
B—Small vesicles	B—Small amount of exudate
C—Sensitive	C—Sensitive
D—No hair removed	D—No hair removed

Conclusions: A satisfactory blistering ointment. The cantharides used in this ointment assayed 0.667 percent cantharidin by the U. S. P. method.

Numerous other lots of ointments made with Chinese Cantharides, containing 0.6% more of cantharidin, have been made and tested physiologically with perfectly satisfactory results.

Practical veterinarians accept blistering ointments made with Chinese Cantharides, and properly labeled, when ointments made with U. S. P. Cantharides are not readily available, and use them with perfect success in their practice.

The tincture and fluidextract of cantharides are also employed, to some extent, externally for rubifacient or vesicant effect, particularly on humans. No specific comparisons of the effects of tincture and fluidextract of U. S. P. and Chinese Cantharides for these purposes were obtained in this investigation, but thousands of pints of properly labeled tincture and fluidextract of Cantharides, some of which was, no doubt, diverted to rubifacient and vesicant use, were used during the period of shortage of U. S. P. Cantharides with perfect success and without complaint of activity. The United States Government also used a considerable quantity of Tincture of Chinese Cantharides during the shortage period.

#### INTERNAL USE.

Cantharides is used internally for its diuretic, aphrodisiac, and emmenagogue effects<sup>3</sup>.

No specific evidence of the comparative values of U. S. P. and Chinese Cantharides, for internal use, was obtained during this investigation, but, as mentioned above, a very large quantity of tincture and fluidextract of Chinese Cantharides was employed with perfect success and with evidently satisfactory activity during the period of shortage of U. S. P. Cantharides, and it appears to be likely that much of these preparations was used for these internal medical purposes. However, the need for scientifically controlled clinical tests is not to be disputed.

#### CANTHARIDIN CONTENT.

The U. S. P. limits the use of U. S. P. Cantharides to that which yields 0.6% or more of cantharidin by the U. S. P. method of assay. No definite standard has been laid down for Chinese Cantharides, but a standard similar to the U. S. P. standard for U. S. P. Cantharides will also insure the use of a satisfactorily active Chinese Cantharides.

Colledge<sup>4</sup> reported a cantharidin content of 1.20% in "Chinese Blistering Fly." Eldred and Bartholomew<sup>5</sup> reported Chinese Cantharides with cantharidin contents of 1.246%, 1.359, and 1.362%, respectively.

Culbreth<sup>6</sup> reported "Chinese Blistering Flies" as containing between 1 and 1.7% cantharidin.

Warner<sup>7</sup> reported a cantharidin content of 0.426% in Chinese Cantharides.

Maisch<sup>8</sup> reported Chinese Cantharides with a cantharidin content of 1.016%.

Fahnestock<sup>9</sup> reported the cantharidin content of Chinese Cantharides as 1.25%.

<sup>3</sup> Culbreth's *Materia Medica and Pharmacology*.

<sup>4</sup> Colledge, W. C., *P. J. & P.*, May 26, 1916, p. 674.

<sup>5</sup> Eldred, F. R. and W. C. Bartholomew, *Proceedings A. Ph. A.*, 1907, p. 360.

<sup>6</sup> Culbreth's *Materia Medica and Pharmacology*, p. 627.

<sup>7</sup> Warner, W. R., *A. J.*, 38, p. 195.

<sup>8</sup> Maisch, *Proceedings A. Ph. A.*, 1872.

<sup>9</sup> Fahnestock, *A. J. P.*, 1839.

Merck's 1907 "Index" gives the cantharidin content of Chinese Cantharides as between 1 and 1.2 percent.

It will be noted that of these figures, only that reported by Warner is lower than the present standard for U. S. P. Cantharides.

These laboratories have corroborated these reports of the higher cantharidin content of Chinese Cantharides. This corroboration is shown by the following data extracted from the Annual Reports of the Committee on Drug Market of the Pennsylvania Pharmaceutical Association, for the years mentioned, which data was contributed to the Reports by these Laboratories:

#### REPORT FOR THE YEAR 1913.

"Chinese Cantharides." Two samples assayed 0.91 and 1.03 percent, respectively, of cantharidin; thus running considerably higher than the variety sold as Russian, which averaged in our Laboratories during the past year 0.604 percent (21 samples).

Powdered Chinese Cantharides differ in appearance from the Russian variety only in color. Aside from this, there would seem to be no reason why the Chinese variety should not be employed as its vesicatory power, as tried out in veterinary practice, is good.

##### *Cantharides, Russian.*

No. of Samples.	Lowest Assay.	Highest Assay.	Average.	Standard.	Above.	Below.
21	0.292%	1.150%	0.604%	0.6% Cantharidin	12	9

#### REPORT FOR THE YEAR 1914

##### *Cantharides, Russian.*

No. of Samples.	Highest Assay.	Lowest Assay.	Average.	Standard.	Above.	Below.
5	0.75%	1.06%	0.91%	0.6% Cantharidin	5	0

Cantharides, Chinese: The 18 lots examined varied between 0.11 percent and 1.95 percent, the average being 1.16 percent Cantharidin.

#### REPORT FOR THE YEAR 1915.

##### *Cantharides, Chinese.*

No. of Samples.	Lowest Assay.	Highest Assay.	Average.	Standard.	Above.	Below.
6	0.570%	1.10%	0.869%	0.6% Cantharidin	5	1

##### *Cantharides, Russian.*

1	0.625%	0.625%	0.625%	0.6% Cantharidin	1	0
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#### REPORT FOR THE YEAR 1916.

##### *Cantharides, Chinese.*

No. of Samples.	Lowest Assay.	Highest Assay.	Average.	Standard.	Above.	Below.
5	1.09%	2.20%	1.46%	0.6% Cantharidin	5	0

#### REPORT FOR THE YEAR 1917.

##### *Cantharides, Chinese.*

No. of Samples.	Lowest Assay.	Highest Assay.	Average.	Standard.	Above.	Below.
6	0.73%	1.14%	0.86%	0.6% Cantharidin	6	0

#### REPORT FOR THE YEAR 1918.

##### *Cantharides, Chinese.*

No. of Samples.	Lowest Assay.	Highest Assay.	Average.	Standard.	Above.	Below.
3	1.08%	1.90%	1.60%	0.6% Cantharidin	3	0

#### REPORT FOR THE YEAR 1919.

##### *Cantharides, Chinese.*

No. of Samples.	Lowest Assay.	Highest Assay.	Average.	Standard.	Above.	Below.
3	0.667%	1.29%	0.933%	0.6% Cantharidin	3	0

The average cantharidin content shown by the 27 lots of Russian Cantharides was 0.713 percent while that of the 43 lots of Chinese Cantharides was 1.123 percent so that as far as Cantharidin content is concerned, Chinese Cantharides is quite superior to U. S. P. Cantharides.

#### PHARMACEUTICAL BEHAVIOR.

The only practical difference in pharmaceutical behavior is influence in the color of the finished products. In powdered condition, as employed in ointments, Chinese Cantharides is brownish in color, whereas Russian Cantharides is greenish brown, and Spanish Cantharides is brownish green. In fluid preparations, the difference in color is more striking, as Chinese Cantharides produces brown preparations, whereas the U. S. P. varieties produce different shades of greenish brown colored preparations. The influence of this difference in pharmaceutical behavior can be eliminated by recognition of the Chinese variety only; by specifying the variety to be used in specific U. S. P. preparations, or by including *Mylabris Cichorii* as a distinct addition to the U. S. P., and as a worthy succedaneum for the present varieties. This latter course finds its precedent in the U. S. P. recognition of ammonium, potassium, and sodium iodides, all of which are employed primarily for their iodide content, and any one of which is a worthy succedaneum for any of the others.

#### PRICE.

Chinese Cantharides has been much cheaper than U. S. P. Cantharides for years. For the past three years, the quotations for Chinese Cantharides have been around \$1.00 per pound, while U. S. P. Cantharides have been around \$4.25 per pound.

#### AVAILABILITY.

The price quotations mentioned above are fair evidence of the ready availability of Chinese Cantharides. During the World War, the ready availability of this variety was more striking, because of the more or less involvement of the countries from which U. S. P. Cantharides are derived in the War, whereas the countries which are the source of *Mylabris Cichorii* were but little affected. The only likely hindrance to availability of this product is involvement of the countries, which are the source of the product, in a great war, but this is as true of the source of U. S. P. Cantharides as of Chinese Cantharides.

#### SUMMARY.

Chinese Cantharides (*Mylabris Cichorii*) is suggested as a worthy candidate for admission to the U. S. P. Its claims for admission are based on the following comparisons with the present U. S. P. varieties:

External Use: Vesicating and rubefacient power is equal to that of the present U. S. P. varieties.

Internal Use: The evidence is offered that the medical profession has employed a tremendous quantity, with apparently perfect success and without complaint of activity. Scientifically controlled clinical comparisons would be preferable to the evidence offered.

Cantharidin Content: On the average, is 50 percent greater than that of the present U. S. P. varieties.

Pharmaceutical Behavior: Similar, except color. Methods of overcoming influence of this difference are suggested.

Price: Chinese Cantharides has been cheaper for years. During the past three years, the price has been only one-quarter as much as U. S. P. Cantharides.

Availability: Enjoys ready availability. Future availability is subject to the same limitations as U. S. P. Cantharides.

PHARMACEUTICAL LABORATORIES,  
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## SHALL WE REORGANIZE THE AMERICAN PHARMACEUTICAL ASSOCIATION?

BY FRANCIS E. STEWART.<sup>1</sup>

It has been suggested that the American Pharmaceutical Association be reorganized and become a delegate body governed by a House of Delegates made up of representatives of the drug trade and proprietary medicine interests; and that the fact be recognized that what we call pharmacy as now carried on is a purely commercial business and that all claims to the contrary are pretense and camouflage.

I am writing this paper to protest against the reorganization of the American Pharmaceutical Association upon any such plan for I believe that such a move would be one of retrogradation. It is, of course, true that what we call pharmacy is not a profession but a commercial business and that the teaching of the colleges of pharmacy in this respect is unwarranted by existing conditions. It is also true that pharmacy has been for centuries unsuccessfully attempting to secure recognition as a profession, and, therefore, further attempts appear to be useless. But I do not believe in giving up the attempt. What we call pharmacy can never obtain recognition as a profession. Until pharmacy becomes a profession in fact professional recognition can never be attained. One of the problems which the American Pharmaceutical Association was organized to solve is how to make pharmacy a profession. It would seem to me far more important for us to unite in a study of the subject for the purpose of solving this important problem than to throw up the sponge and acknowledge ourselves vanquished by reorganizing the A. Ph. A. and making it a commercial body.

It has always been my opinion that the reason why we have never succeeded in solving the problem is because we have never gone about it in the right way. Pharmacy is inherently and historically a branch of medical science and practice and, therefore, can never become a profession independently of the medical profession. As well cut off a man's head and expect his body to go around and attend to business as to expect pharmacy to exist as an independent profession.

We should, therefore, turn to the history of the medical profession to learn about the true professional ideal in relation to pharmacy. I am suggesting the study of the *history* of the medical profession rather than to hold up the profession as it now exists as an ideal for us to follow. The medical profession is becoming "commercialized" and is forgetting the true professional ideal. The medical pro-

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<sup>1</sup> A Committee on Reorganization, consisting of F. E. Stewart, *Chairman*, J. A. Koch and S. L. Hilton, was appointed by President L. E. Sayre.