

Working Directions.—Triturate the carmine with the stronger ammonia water until solution is effected. Add this to the silver nitrate, previously pulverized, and stir well. To this add the potassium bitartrate and again stir briskly. Next add the syrup which causes the mixture to become quite viscid. Finally add the mucilage of acacia, and the mixture is completely homogenized by thorough shaking. The result is a deep purplish red ink, which prints light red letters.

Method of Using.—Before the dressings are introduced into the sterilizer a piece of paper, upon which is written with the sterilizing ink the date of sterilization, is attached to the dressings. The sterilizing is conducted in the usual way. If sterilizing temperature (approximately 260° F.—20 pounds pressure) is attained, when the dressings are withdrawn the ink upon the paper which was originally red, will have changed to a black color, indicating the completion of proper sterilizing technique.

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FURTHER NOTES ON TINCTURE OF CANTHARIDES.*

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As the U. S. P. process for Tincture Cantharides, as well as the process referred to in my paper presented to this Section in 1919,¹ do not always yield satisfactory results, further experiments have been made on the extraction of cantharides with the view of finding a simple method and suitable menstruum which will yield uniform and satisfactory results.

This paper should be considered in connection with my two previous papers on this subject,¹ and is not intended as a final report, but is offered for the purpose of recording the experiments which have been made and the results obtained. These experiments seem to indicate that it will be possible to prepare a Tincture of Cantharides by a simple extraction process, *i. e.*, the ordinary cold percolation method, with a menstruum that may prove acceptable for this preparation.

It has been claimed that glacial acetic acid, chloroform and acetone are excellent solvents for cantharidin, to which the activity of this drug is ascribed. Two preliminary experiments were therefore made, as follows:

Experiment No. 1.—100 Gm. of Powdered Cantharides were moistened, macerated for two days, and then percolated to obtain 1000 cc of tincture, using a mixture of 1 vol. of glacial acetic acid and 9 vols. of alcohol as a menstruum.

Experiment No. 2.—100 Gm. of Powdered Cantharides were moistened, macerated and percolated with acetone until exhausted; the acetone was then distilled off and the residue dissolved in alcohol to make 1000 cc.

Both tinctures were tested for blistering power by application to the skin of the arm. The tincture obtained in Experiment No. 1 produced a blister; the tincture obtained in Experiment No. 2 reddened the skin, but produced no blister.

A lot of Powdered Cantharides (assaying 0.9975% total cantharidin) was then set aside for further experiments, which were carried out as follows:

* Read before Section on Practical Pharmacy and Dispensing, A. Ph. A., Cleveland meeting, 1922.

¹ JOUR. A. PH. A., 8, 1030, 1919, and 10, 705, 1921.

Experiment No. 3.—100 Gm. of drug were moistened with 100 cc of chloroform, macerated in a well-stoppered flask for twenty-four hours, and then percolated with alcohol to obtain 1000 cc of tincture.

Experiment No. 4.—100 Gm. of drug were moistened with 100 cc of a menstruum consisting of 1 vol. of chloroform and 9 vol. of alcohol, macerated in a well-stoppered flask for twenty-four hours, then packed in a percolator and percolated with the same menstruum until 1000 cc of tincture had been obtained.

Experiment No. 5.—100 Gm. of drug were moistened with 100 cc of glacial acetic acid, macerated in a well-stoppered flask for twenty-four hours, then packed in a percolator and percolated with alcohol to obtain 1000 cc of tincture.

Experiment No. 6.—100 Gm. of drug were moistened with 100 cc of a menstruum consisting of 1 vol. of glacial acetic acid and 9 vol. of alcohol, macerated in a well-stoppered flask for twenty-four hours, then packed in a percolator and percolated with the same menstruum until 1000 cc of tincture had been obtained.

Experiment No. 7.—100 Gm. of drug were moistened with a mixture consisting of 50 cc of glacial acetic acid and 50 cc of alcohol, macerated in a well-stoppered flask for twenty-four hours, then packed in a percolator and percolated with alcohol until 1000 cc of tincture had been obtained.

Experiment No. 8.—100 Gm. of drug were moistened with 100 cc of menstruum consisting of a mixture of 1 vol. of glacial acetic acid and 19 vol. of alcohol, macerated in a well-stoppered flask for twenty-four hours, and then packed in a percolator and percolated with more of the same menstruum until 1000 cc of tincture had been obtained.

Tinctures made with the use of glacial acetic acid are slightly darker than regular U. S. P. tincture obtained from the same drug, but lighter than those obtained with the use of chloroform.

All of these tinctures were tested for blistering power, after they had aged several months, by applying a drop of tincture which had previously been concentrated to about one-fourth of its volume, to the skin of the forearm. The tincture obtained from Experiments Nos. 4, 6, 7 and 8 produced good blisters. Tinctures obtained from Experiments Nos. 3 and 5 produced reddening of the skin. The latter two were tried again and a blister was obtained on the second trial.

The tinctures were also assayed, using the clear tincture after aging for three months. This procedure was followed as it was thought that some precipitation might possibly occur on standing, and it was desired to determine the strength after aging and clarification. No appreciable sediment, however, was noticeable in any of the tinctures, except No. 5, which showed a trace of sediment adhering to the bottom of the bottle.

It will be noted that tinctures in which glacial acetic acid was used as an aid to extraction assayed higher than those in which chloroform was used in the same manner. It will further be noted that the U. S. P. tincture gave the lowest assay of all.

As the drug that was used in all of the above experiments was from the same lot, the assay results indicate which menstruum is most likely to give the best results.

For purpose of comparison, a liter of tincture was produced from the same lot of drug by both the U. S. P. process and the process given in my paper of 1919. These were also tested for blistering action, as well as assayed, with results shown in the table.

TABULATION OF EXPERIMENTS.

Expt. No.	Drug moistened with	Drug extracted with	Final composition of tincture aside from drug extractive.	Blister- ing action.	Assay. 100 cc.
1	Glac. acet. acid 1 vol. Alcohol 9 vols.	Glac. acet. acid 1 vol. Alcohol 9 vols.	Glac. acet. acid 1 vol. Alcohol 9 vols.	†	Not assayed
2	Acetone	Acetone	Alcohol	§	Not assayed
3	Chloroform	Alcohol	Chloroform 1 vol. Alcohol 9 vols.	‡	0.046 Gm.
4	Chloroform 1 vol. Alcohol 9 vols.	Chloroform 1 vol. Alcohol 9 vols.	Chloroform 1 vol. Alcohol 9 vols.	†	0.0666 Gm.
5	Glac acet. acid	Alcohol	Glac. acet. acid 1 vol. Alcohol 9 vols.	‡	0.100 Gm.
6	Glac. acet. acid 1 vol. Alcohol 9 vols.	Glac. acet. acid 1 vol. Alcohol 9 vols.	Glac. acet. acid 1 vol. Alcohol 9 vols.	†	0.0895 Gm.
7	Glac. acet. acid 1 vol. Alcohol 1 vol.	Alcohol	Glac. acet. acid 1 vol. Alcohol 19 vols.	†	0.0780 Gm.
8	Glac. acet. acid 1 vol. Alcohol 19 vols.	Alcohol 19 vols. Glac. acet. acid 1 vol.	Glac. acet. acid 1 vol. Alcohol 19 vols.	†	0.090 Gm.
9	*	Alcohol	Alcohol	‡	0.0385 Gm.
10	**	Potass. hydroxide U. S. P. 0.68 Gm. Water 30.00 cc Alcohol 70.00 cc	Alcohol 7 vols. Water 3 vols.	§	0.0421 Gm.

* U. S. P. process (hot maceration for twenty-four hours, then percolate).

** Dr. Squibb's process (cold maceration for 1 week, then percolate).

† Blister on one application.

‡ Blister on second application.

§ No blister.

The results indicate that a tincture produced by extraction with alcohol with the aid of acetic acid may prove satisfactory if no objection can be raised against the presence of the acetic acid in the preparation and thereby solve the difficulties encountered in the past with the complete extraction of this drug.

It is my intention to have further experiments made for the purpose of determining the smallest amount of acetic acid that will prove satisfactory, as well as whether or not this method will yield uniform results, which is not the case with either of the U. S. P. IX or the alkaline extraction methods.

ABSTRACT OF DISCUSSION.

W. L. Scoville referred to his work on the same subject. (See *Proceedings A. Ph. A.*, 1910, p. 1115; *Jour. A. Ph. A.*, Volume II, p. 18; Volume III, p. 631; Vol. VI, p. 798.) He agreed with Mr. Nitardy that acetic acid and alcohol gave the best results. He could not see the force of objections to acetic acid in Tincture of Cantharides.

It was voted that this paper be referred to Chairman George M. Beringer, of Sub-Committee No. 11, U. S. P. Revision Committee.

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