TINCTURE OF CANTHARIDES.*

(FOURTH PAPER.)

BY WILBUR L. SCOVILLE.

In 1910 I called the attention of this Section to the fact that the U. S. P. Tincture of Cantharides does not adequately represent the drug, the alcohol extracting usually less than half of the cantharidin present. Also that a menstruum consisting of 10 volumes of glacial acetic acid and 90 volumes of alcohol makes a very satisfactory tincture. In the discussion it was stated that 10 percent of acetic acid was objectionable, although I pointed out that for external use this increased the activity of cantharides, and if taken internally the amount of acetic acid in 5 minims of tincture would correspond to about 8 minims of table vinegar.

In 1913 a second paper was presented giving the results obtained with menstrua composed of alcohol-chloroform, alcohol-acetone and alcohol-acetic ether, each with small amounts of acetic acid to liberate any combined cantharidin which might be present. The results shown with these varied from 26 percent to 74 percent of the drugs taken—a less satisfactory conclusion than was obtained in the experiments of the first paper.

In 1914 a third paper was presented giving results obtained by digesting the drug, first with boiling water containing a little acetic acid, then after partial cooling adding chloroform-alcohol or acetone-alcohol or acetic-ether alcohol, macerating for a day or two, then filtering. The proportions of water were adjusted so that the final tinctures were clear and homogeneous, neither water nor chloroform being in excess. By using chloroform-alcohol in this manner, one tincture was obtained which represented 100 percent of the drug used, but several subsequent attempts to repeat this success resulted in disappointment.

These tinctures represented mostly 75 percent to 85 percent of the drug taken.

The net result of the three papers is to show (1) that alcohol alone is not sufficient as a menstruum for cantharides because it does not extract even to saturation, and also because cantharidin is so little soluble in alcohol that even a saturated alcoholic solution cannot represent high-grade drugs which are in the market; (2) that digestion favors extraction and that hot water has peculiar advantages in this respect; (3) that some better solvent than alcohol is needed, either alone or in conjunction with alcohol as a menstruum; and (4) that cantharides are especially difficult to extract with any solvent.

There remained one other process to try, and this forms the substance of the present paper, namely, the extraction of the drug with a suitable menstruum and mixing this extract with sufficient alcohol to make a tincture.

Since acetic ether (ethyl acetate) is probably the least objectionable of the good solvents, this was used in all experiments.

The process used consisted in exhausting the cantharides (100 Gm.) in a Soxhlet apparatus with about 150 mils of acetic ether to which 5 mils of glacial acetic acid was added, adjusting the volume of the extract to 150 mils and then adding sufficient alcohol to make 1000 mils.

The tincture thus represented 10 percent of drug in a menstruum containing,

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by volume, 0.5 percent of acetic acid, 15 percent of acetic ether and alcohol to 100 percent.

Extraction with the acetic ether was continued until a few drops yielded no residue on spontaneous evaporation. It was found that 12 to 18 hours' extraction was required in most cases—the finer the drug the less the time required. In practical work more than 150 mils of the ether was required to saturate the drug and secure a flow in the Soxhlet without driving out all of the ether from the receiver before the flow recurs. Sometimes the volume of extract exceeded 150 mils by a small amount, sometimes it was less, and in order to secure uniformity in the tinctures the volume was adjusted, by evaporation or dilution, to 150 mils.

This was then poured into about 800 mils of alcohol, and the container rinsed with enough alcohol to make 1000 mils. A small amount of precipitate formed on mixing, and after standing 24 hours the tincture was filtered. Except for slight fat-deposits, of a semi-crystalline character, the tinctures have remained clear.

Drug A, contained 1.08 percent cantharidin and produced a tincture assaying 0.090 percent, representing 83 percent of the drug.

Drug B, contained 0.90 percent cantharidin and produced a tincture assaying 0.084 percent, representing 93 percent of the drug.

Drug C, contained 0.75 percent cantharidin and produced tincture assaying 0.071 percent, representing 95 percent of the drug.

A sample of U. S. P. IX tincture was also made from Drug C and assayed 0.010 percent of cantharidin, or only 13 percent of the drug was represented in the tincture.

Probably a small allowance for loss in the tincture must be made on account of the evaporation during the process of assay, cantharidin being slightly volatile even at room temperatures, but the last tincture certainly does not look well.

It is again evident that some solvent beside alcohol is needed for the extraction of cantharides. Of the solvents suitable, boiling water is efficient so long as it is boiling, but it is no longer a solvent when it is cold. Acetone is effective, but is not suitable for internal use. Glacial acetic acid is both rapid and effective, and for ordinary extraction by percolation is the most promising. Chloroform is probably the most ready solvent, but is more objectionable in the tincture than is ethyl acetate which extracts more slowly but which has proved sufficient for the purpose. Undoubtedly tinctures representing at least 90 percent of the drug can be made by extracting first with acetone or chloroform, and mixing this extract with alcohol.

The mixture of 10 volumes of glacial acetic acid with 90 volumes of alcohol has the advantage that it exhausts the drug by the ordinary process of percolation—if conducted slowly. It produces a tincture which is satisfactory physically, and is but about half as strong again in acetic acid as the old line of *aceta*. If used externally the acetic acid acts as an adjuvant—promoting and perhaps intensifying the action of the cantharides. If used internally the dose is so small that much less acid is taken than in other *aceta*, and the acid property cannot be considered as seriously objectionable. The internal administration of about 8 minims of table vinegar—which would be equal to the acid in 5 minims of such tincture—is ordinarily a matter of indifference.

The other alternative is to extract the drug first with ethyl acetate or chloroform, preferably in a continuous extraction apparatus, and with sufficient acetic acid to free all combined cantharidin, and then mix this extract with sufficient alcohol to produce the tincture.

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BOTANICAL NOMENCLATURE OF THE N. F. IV.*

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A careful examination of the botanical nomenclature adopted in the National Formulary IV shows that it follows in part the Vienna Code and in part the American Code, with a strong leaning toward the latter as the predominant feature. The adoption of the trinomial system is to be deprecated, as it makes the authors express an opinion which they had never for a instant entertained. The trinomial system under the American Code is the method of expressing a subspecies, the "Code" not recognizing the rank of variety. Yet in every instance where the trinomial is used the author quoted did not publish a subspecies; he published a variety. Geographical names are decapitalized; as they are proper names they should be capitalized the same as is done with other proper names. The following notes and comments may be of service in the next revision:

Agaricus.—Derived from *Polyporus officinalis* Fries. This is not the valid name for the fungus producing the white agaric used in medicine. Winter, in the second edition of Rabenhorst's Kryptogamen Flora, uses the above name; Murrill, in North American Flora, uses the combination *Fomes Laricis* (Jacq.) Murrill; Hennings, in Engler u. Prantl's Pflanzenfamilien, adopts both *Fomes* and *Polyporus* as distinct genera, but unlike Murrill refers the white agaric to *Polyporus* as *P. officinalis*. The species of *Fomes* are, perhaps, by most authors regarded as species of *Polyporus*, but whether *Fomes* or *Polyporus*, the oldest and valid specific name is *Laricis*. The proper name under *Polyporus* is *P. Laricis*. The proper name under *Polyporus* is *P. Laricis* (Jacq.) Scopoli.

Asarum.—Hyphenated words are rapidly going out of favor, the word being written as either one word or two distinct words; "snakeroot" is the most generally accepted way of writing the word, not "snake-root."

Cactus Grandiflorus.—The botanical origin is given as *Cactus grandiflorus* Linné, with the synonym *Cereus grandiflorus* Miller. These names certainly appertain to the drug known commercially as "cactus grandiflorus," but they are only synonyms and should not be used, especially the Linnæan name, for the plant producing the drug has not been classed in the genus *Cactus* by any botanist for nearly a century and a half. The proper name for this drug is *Selenicereus grandiflorus* (Lin.) Britton and Rose. In the third line of the description on page 275 the words "each about 2 mm." would be more accurate if changed to read "5 mm. or less," and the word "spines" after "flexuous" should be changed to "bristles." It may not be out of place to note here that a related Mexican species, the *Selenicereus pteranthus* (Link and Otto) Britton and Rose, has been used as a substi-

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