2. Heat favors extraction, but has less effect in anhydrous than in hydrated menstrua.

3. The best menstruum thus far found is a mixture of one volume of glacial acetic acid with nine volumes of alcohol.

4. Mixtures of water, alcohol and chloroform, acidulated with acetic or hydrochloric acid have given good results in some cases, but the proportions and method which will give uniformly satisfactory results have not yet been discovered.

PARKE, DAVIS & Co., Detroit, Mich.

DISCUSSION.

Otto Raubenheimer, of Brooklyn, said Mr. Scoville's work was certainly a valuable one, and proved without doubt that the Brussels International Conference had made a mistake when they made the international agreement that tincture of cantharides should be made 10 percent strength. Instead of using a menstruum of 70 percent alcohol by percolation, Mr. Scoville recommended making a glacial acetic acid menstruum, which seemed to extract the cantharidin and made a 100 percent tincture, by mixing one part of glacial acetic acid with nine parts alcohol. He thought this was a good means of extracting the cantharides. But at the same time it was doubtful whether it could be used, because frequently tincture of cantharides was administered internally, and especially as a veterinary remedy, for horses and cattle. He thought this formula was objectionable because of its high percentage of glacial acetic acid.

Mr. Scoville responded to this that in the official dose of tincture of cantharides the equivalent would be given. For instance, 5 minims tincture cantharides made with acetic menstruum equals 8 drops of ordinary vinegar; so even with a horse or other animal, where a relative amount was given, he did not see how it could be objectionable.

F. T. Gordon, of Philadelphia, wanted to know the effect of cantharides used as a hair tonic, and Mr. Scoville responded humorously that it was "a psychological effect only," inasmuch as there was no cantharidin really in these remedies.

L. F. Kebler, of Washington, D. C., wanted to know of Mr. Scoville on what basis he made the statement that the present pharmacopœial tincture of cantharides was misbranded, in view of the fact that this was recognized as standard in the Federal Food and Drugs Act.? The law declared that if it was prepared in accordance with the pharmacopœial method, it was a proper standard. He remarked that the results here stated brought to mind the possible reason why so many hair-tonics, said to be made with cantharides, had failed. He thought it was worth while to investigate this subject, for the benefit of mankind in general.

## DETERMINATION OF SANTONIN IN SANTONICA.

CHARLES E. CASPARI, ST. LOUIS.

During the past winter, the fact was brought to my attention that Santonica was being bought and sold on its santonin assay, in fact, a certain manufacturer of stock remedies was in the market for Santonica with a guaranteed santonin content, claiming that he had always been able to procure such. At that time I knew of no published method for the determination of santonin and after correspondence and conversation with a number of my pharmaceutical-chemical friends, I learned that they knew no more than I did about the determination of santonin. I discovered that a firm of crude drug dealers in Chicago was assaying Santonica, but when I applied to that firm and requested it to give me

the method of assay, my request was politely but firmly refused, on the ground that this firm intended to take up the manufacture of santonin on a large scale and that its assay method would be the manufacturing process, which it desired to keep secret. About this time, our presiding officer, Mr. Frank R. Eldred, whom I take this opportunity of thanking, as well as the firm with which he is connected, Eli Lilly & Co., called my attention to three articles published in the Archiv der Pharmazie by Thaeter in Vol. 235, page 401 and Vol. 237, page 626 and by Katz in Vol. 237, page 245. Katz's article is a criticism of Thaeter's first article and some suggested improvements and Thaeter's second article is a reply to Katz.

I carefully and conscientiously endeavored to apply both the methods of Katz and Thaeter to the determination of santonin, but with very unsatisfactory results. Some santonin was always obtained, but an indeterminate amount was always lost on account of the large amount of resin that was precipitated with the santonin and the difficulty of separating the santonin quantitatively from the resin, so that it was impossible for me to obtain duplicate results that checked. About this time, my father, Charles Caspari, Jr., referred me to an article by Fromme, published in the Jahres-Bericht of Cæsar & Loretz of Hallé for September, 1912, for the determination of santonin in Santonica, which is a modification of Katz's method and which gave very satisfactory results. I take this occasion to say that I make absolutely no claim of originality in this paper, but merely desire to call the attention of the pharmaceutical-chemical profession to a quantitative method which I am sure is little known and which gives good results.

The method of Fromme follows: Thirteen grams of moderately finely powdered wormseed are placed in a separatory funnel containing 130 grams of chloroform. A pledget of cotton should be placed in the funnel above the stopcock before introducing the wormseed. After one hour's maceration with occasional shaking, 102.5 grams (equal to 10 grams of drug), of the liquid are drawn off into a 200 c. c. Erlenmeyer flask. Evaporate the chloroform until the residue weighs 7 to 8 grams. Add 100 grams of five percent barium hydroxide solution and place the flask in hot water. After the chloroform has evaporated sufficiently to enable the resin to rise to the surface, it is heated until all odor of chloroform has disappeared. Filter through a plain filter of six cm. diameter, previously wetted, into a 200 c. c. Erlenmeyer flask; rinse the flask and filter twice with 10 c. c. of hot water, add five grams of twenty-five percent hydrochloric acid to the filtrate and heat the whole for several minutes on a boiling water bath. After the liquid has been cooled somewhat by setting the flask in cold water, pour the liquid into a separatory funnel and rinse the flask with twenty c. c. of chloroform, which is added to the contents of the funnel. Shake the mixture actively for two minutes and after the chloroform has separated perfectly, filter the same through a double plain filter into a 100 c. c. Erlenmeyer flask. Wash the acid-aqueous liquid twice with fifteen c. c. of chloroform by agitation and draw the chloroform off as before through the filter. Distil the chloroform from the combined filtrate and remove the last traces of chloroform from the residue by a current of warm air. Dissolve the residue in 7.5 grams of absolute alcohol and add 42.5 grams of hot distilled water. Filter the milky

liquid at once into a tared 100 c. c. Erlenmeyer flask and wash the flask and filter twice with ten grams of a mixture of three grams of absolute alcohol and seventeen of distilled water. Set the filtrate aside for 24 hours (not longer) and filter through a plain six cm. tared filter, washing the flask and filter twice with ten grams of the above alcohol-water mixture. Dry the flask and filter at 100 degrees C. to constant weight, place in a desiccator for one-half hour and weigh again. To the weight of the santonin thus found add 0.04 gram for loss by solution in the dilute alcohol. The total weight of santonin multiplied by ten, gives the percentage content, which should be calculated on the basis of previously dried wormseed.

It may not be out of place to say a word in explanation of Fromme's method. Santonin is the inner anhydride or lactone of santoninic acid and probably occurs as such in the wormseed. The extraction with chloroform removes the santonin and considerable resin, while the treatment with barium hydroxide converts the santonin into barium santoninate, at the same time that the barium salt of certain resin acids is formed. The addition of hydrochloric acid sets free santoninic acid and also some resin acids. The heating on the water bath for several minutes serves to convert the santoninic acid into the lactone, santonin. This, together with some resin acids, is extracted from the acid liquid with chloroform and the chloroform is then evaporated. The residue is dissolved in absolute alcohol and enough hot water is added to make the alcohol fifteen percent strength, because it was found by experiment that alcohol of this strength was best adapted to dissolve the santonin while hot and to hold the least amount in solution when cold. When the alcoholic solution cools, the santonin separates out in crystals, while the resins separate out in such a fine state of division that they pass through the filter paper with the greatest ease. The addition of 0.04 gram to the amount of santonin obtained is made necessary because that amount of santonin is held in solution by the amount of fifteen percent alcohol used. In order to obtain concordant results, it is necessary to adhere rigidly to the amounts given in the method.

I have tried this method on two samples of Santonica, and, as stated above, I obtained very satisfactory results. The method is infinitely superior to that of either Thaeter or Katz. The results which I obtained on the two samples of Santonica were Sample No. 1, 2.09% and 2.21% and Sample No. 2, 2.46% and 2.33%. I have not had time to make more determinations, but the method worked so satisfactorily that I see no reason why it should not prove successful in the hands of any chemist.

In Vol. II, page 596, of the Journal of the American Pharmaceutical Association, LaWall calls attention to the fact that there is Santonica on the market which is practically devoid of santonin, and I wish to confirm this fact. There are large quantities of wormseed being imported into this country, in which the amount of santonin cannot be considered as more than the faintest trace and it is practically impossible to differentiate by inspection between the true and the spurious. Hence, it becomes necessary to have recourse to the quantitative method for the determination of santonin and fortunately we have a satisfactory method in the one of Fromme described above. It would seem desirable that this method be adopted by the government at the various ports of entry of this

country and that it also be incorporated in the forthcoming United States Pharmacopœia.

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DISCUSSION.

Clement B. Lowe, of Philadelphia, said that large quantities of crude santonin were being imported into this country, and he wanted to know whether it was possible that this santonica which seemed to yield no santonin had been treated, or could be treated, without altering the physical appearance of the drug. He was aware that this had been done with some drugs, as with opium, for instance, where a part of the morphine content had been abstracted and then the drug fixed up from that.

Prof. Caspari said it was true, that large quantities of crude santonin were imported, but the source was controlled by the Russian government, a close corporation, and he did not believe that the santonica that came in devoid of santonin had been subjected to treatment in the old country. Dr. H. H. Rusby had told him that the spurious article was a different species. Tons of this spurious species were being used all over the country, especially for stock-powders, which were absolutely worthless.

Hermann Engelhardt, of Baltimore, made the comment that out of ten samples of santonica he had examined, he had found nine with no trace of santonin whatever. He expressed the opinion that all of the tests given were uncertain.

Chairman Eldred said that, while it did not bear upon the determination of santonin, he was reminded to say that the representative of a drug importer had told him a few months before that he had considered the handling of santonin, and had gone to Russia to investigate the conditions of the market there, and he had found it just as Mr. Caspari has stated, that it was a very close corporation. An interesting fact was, that some of the growers were paid for their drug, which was then set fire to and burned in the fields, in order to keep from overloading the market with santonin.

## DETECTION AND ESTIMATION OF MINUTE QUANTITIES OF FORMALDEHYDE IN PRESENCE OF HEXAMETHYLENAMINE AND OF METHYL ALCOHOL IN PRESENCE OF ETHYL ALCOHOL.

H. A. B. DUNNING, BALTIMORE.

Sometime during the year 1912, Dr. Curtis F. Burnam, member of the staff of Johns Hopkins Hospital, sought my advice as to the most satisfactory method of detecting traces of formaldehyde in urine.

After a careful investigation, I recommended, as most delicate and satisfactory, three tests herein named and described.

Only one of these tests, Rimini's, was of particular value in his work on account of the presence of hexamethylenamine in the material tested. Hehner's milk test, while most delicate, was not suitable on account of being conducted in acid solution, resulting in decomposition of hexamethylenamine with the production of formaldehyde.

While Rimini's test has been found to be most satisfactory in differentiation of formaldehyde in presence of hexamethylenamine, experience teaches that certain precautions should be observed to obtain best results.

The specimens to be examined and all test solutions should be warm, not hot,