

the lead dish the least. Determinations were repeated in the lead dish and results varying from -0.16 per cent to -0.33 per cent were obtained. None of the dishes gave results sufficiently accurate so as to justify their use in the method.

DISCUSSION.

From the experimental work reported in this paper it may be plainly seen that the official method for the determination of camphor in camphor liniment is far from accurate. The method as described in the U. S. P. X is a method which will give results sometimes more than one per cent low. Any such method is objectionable in enforcement of the Pure Food and Drugs Act. The amount of this oxidation depends upon a number of factors, such as time of heating, kind and size of dish, temperature of heating and amount of air present during heating.

CONCLUSIONS.

1. A critical study of the U. S. P. method for determination of camphor has been made.
2. The method has been found to give consistently low results.
3. The error in this method is due to the oxidation of the olein in the cotton-seed oil.
4. Various kinds of dishes and various methods of heating have been used, but none of these have proved satisfactory.

A more satisfactory method has been developed for this determination by the use of the vacuum oven and will be reported in a later communication.

STATE FOOD AND DRUG LABORATORY AND
DIVISION OF SANITARY CHEMISTRY,
COLLEGE OF PHARMACY, UNIVERSITY OF COLORADO,
BOULDER, COLORADO.

THE PREPARATION, ANALYSIS AND LEAD-ION CONCENTRATION OF SOLUTIONS OF COLLOIDAL LEAD.*

BY H. S. KEELAN, R. B. SMITH AND W. G. CHRISTIANSEN.

During the course of some work on the preparation of colloidal lead for cancer therapy some observations have been made which are of interest in connection with this problem.

When it was found that colloidal lead solutions which had been prepared without the use of anaerobic technique throughout turned white upon boiling for sterilization, the procedure to be described was developed and found to be entirely satisfactory. The water used for all purposes during the preparation of the colloidal solution was boiled for half an hour, covered with an inch layer of liquid petrolatum and cooled. Where any water was needed, it was siphoned from beneath the oily layer. The granulated lead to be used was exhausted of air by putting it into a vacuum desiccator, evacuating the latter and breaking the vacuum with nitrogen; the process was repeated three times.

One hundred and sixty cc. of a 1% gelatin solution, 148 cc. of a solution containing 1 mg. of potassium chloride per cc. and 92 cc. of water were put into

* Scientific Section, A. Ph. A., Portland meeting, 1928.

a liter beaker and covered with 300 cc. of liquid petrolatum. Enough granulated lead was then added to form a layer a quarter of an inch thick on the bottom of the beaker. The liquid in the beaker was stirred slowly, using a mechanical agitator; rapid agitation causes the arcs which are to be produced to break. Using lead rods and a 110-volt D. C., the lead was sparked for fifteen minutes and the resulting solution was transferred to centrifuge tubes by means of a pipette; by introducing some liquid petrolatum into the tubes, the aqueous solution can be pipetted from beneath the liquid petrolatum in the beaker and run under the oil in the tube. After the solution has been centrifuged for four minutes at 1200 r. p. m. it is poured into a 400-cc. beaker containing 100 cc. of liquid petrolatum.

The ampuls to be filled with this solution were placed in a vacuum desiccator and the latter was evacuated and filled with nitrogen several times. The ampuls were then quickly removed from the desiccator and stuck down through the liquid petrolatum layer into the colloidal lead solution. The beaker containing the solution and inverted ampuls was then placed in a vacuum desiccator and the desiccator was evacuated so that about half the nitrogen in the ampuls had been removed. The vacuum in the desiccator was then broken with nitrogen and the colloidal solution rose in the ampuls. The latter were then quickly lifted from the beaker and sealed in a gas flame. The solution was then sterilized by autoclaving the ampuls for half an hour at ten pounds steam pressure. The lead content of these solutions was 5 to 6 mg. of lead per cc.

These lead solutions were injected into cancerous patients with more or less negative results. The preparation was not toxic, and the patients suffered none of the bad reactions, such as chills, etc., which have been described in the Blair Bell publications. An interesting observation was noted upon administration of a solution which was made from water which had been boiled the night before and sealed from air immediately with liquid petrolatum as usual. When the patient was injected with this solution, the cancer cells broke down so rapidly that blood was found in the urine, and a blood transfusion was necessary to save the patient. Inasmuch as the solutions obtained by use of freshly boiled water did not produce such rapid disintegration of the cancerous tissue as that noted in the case just referred to it may be that the water should be allowed to stand for a certain length of time prior to use. One normal sample which had aged twelve days prior to use caused a patient to have chills, but this was noted in none of the other samples less than twelve days old.

Experiments were made to determine whether liquid petrolatum exerted any effect other than that of protection against air. It was noticed that at the water-oil interface there was a scum suggesting that the insoluble impurities of both the oil and water phases had collected there. Solutions of lead acetate, with known quantities of lead present were treated with liquid petrolatum both with violent agitation and with the slow stirring used in the regular process. There was a loss of lead from the aqueous phase amounting to 20.5% in the first case and 8.2% in the second.

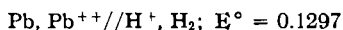
ANALYSIS OF COLLOIDAL LEAD SOLUTIONS.

Five cc. of the standard lead solution (1-Gm. lead-acetate crystals per liter) were diluted to 90 cc. with water in a 100-cc. graduate, 100 mg. of sodium acetate,

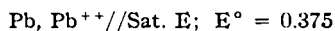
and then 10 cc. of saturated hydrogen-sulphide solution were added to produce the brown coloration. Ten cc. of the unknown colloidal lead solution were treated with 0.4 cc. of glacial acetic acid (excessive quantities of the acid cause the brown color of the sulphide solution to be incorrect) and shaken until a clear solution is obtained; the solution was diluted to 100 cc. in a volumetric flask. One cc. of this solution was put into a 100-cc. graduate and diluted to 90 cc.; 500 mg. of sodium-acetate crystals were added followed by 10 cc. of hydrogen-sulphide water. The depth of colors of the standard and unknown solutions were compared in a colorimeter.

LEAD-ION CONCENTRATION OF COLLOIDAL LEAD SOLUTIONS.

Lewis and Brighton¹ determined the voltage of the normal lead electrode with respect to the normal hydrogen electrode and for the chain



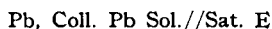
In our study of colloidal lead the measurements were made with a saturated half cell and for this chain



Adopting the procedure of expressing the hydrogen-ion concentration of a solution as the negative logarithm of the H-ion concentration, *i. e.*, p_{H} , we have expressed the lead-ion concentration of a solution in terms of p_{Pb} . When a saturated half cell is used this may be calculated according to the following equation.

$$p_{\text{Pb}} = \frac{E - 0.375}{0.02955}$$

Lewis and Brighton¹ state that lead being a soft ductile metal gives steady and reproducible readings against solutions of its ions; our work confirms this statement. The above authors found that the lead amalgam electrodes gave somewhat better results than solid lead electrodes; since the amalgam would dissolve lead from the colloidal lead solutions and thereby change in composition, these electrodes were not investigated. The electrodes used were bars of C. P. lead about 7 mm. in diameter which were scraped with a sharp-edged piece of glass and then burnished with a piece of glass rod immediately before being placed in the solution. The solutions were stirred with nitrogen while the determinations were being made. The following chain was used.



In order to reduce the diffusion of salts from the salt bridge into the colloidal lead solution a *N*/10 KI salt bridge was used between the colloidal lead solution and the saturated half cell.

It was found that there were no great differences between the lead-ion concentrations of preparations made by the method described in the first part of this paper. The p_{Pb} was found to vary from 8.74 to 10.28 which corresponds to lead-ion concentrations of 1.8×10^{-9} to 5.3×10^{-11} . It was also found that the lead-ion concentration was not altered by sterilization of the ampuled solution as described above.

In every case during the preparation of the colloidal lead a white material

¹ Lewis and Brighton, *J. A. C. S.*, 39 (1917), 1906.

appeared at the oil-water interface, and it was thought that this material and not the colloidal lead might be determining the lead-ion concentration of the solution. It was further noted that when air instead of nitrogen was passed through a colloidal lead solution a heavy white precipitate slowly developed which was similar in appearance to that which had been noted at the oil-water interface. Under these later conditions Pleissner¹ has shown that $2 \text{PbCO}_3 \cdot \text{Pb(OH)}_2$ is formed. A colloidal lead solution which had been found to have a p_{Pb} of 9.06 was aerated for $1\frac{3}{4}$ hours; after this treatment the resulting solution was almost white and the p_{Pb} had dropped to 8.39, *i. e.*, the lead-ion concentration had increased from 8.7×10^{-10} to 4.1×10^{-9} .

A sample of $2 \text{PbCO}_3 \cdot \text{Pb(OH)}_2$ was prepared by mixing solutions of lead acetate and ammonium carbonate and converting the lead carbonate into the basic salt by repeatedly boiling with water, washing with cold water and again boiling with water. The final preparation was boiled and cooled in a vacuum. The p_{Pb} of the saturated solution at 25°C . was 3.96 which is equivalent to a lead-ion concentration of 1.1×10^{-4} .

Various values for the solubility of $2 \text{PbCO}_3 \cdot \text{Pb(OH)}_2$ are given in the literature and it is possible that these variations may be due to varying CO_2 pressure which changes the solubility of the basic carbonate. One of the best values is that given by Auerbach and Pick² in terms of the solubility product, *i. e.*, 3.5×10^{-46} . A saturated solution of the pure salt containing no excess of any of the ions would therefore be equal to $\sqrt[2]{3.5 \times 10^{-46}}$ or 7.6×10^{-3} . The value found for the pure salt by the lead-ion concentration method as given above was 1.1×10^{-4} . A saturated solution of Pb(OH)_2 has a solubility product variously given as 0.82×10^{-15} and 0.47×10^{-15} to 0.91×10^{-5} .

The lead-ion concentration of these salts could not, therefore, be less than 10^{-6} so that it could not be either basic lead carbonate or lead hydroxide which determines the lead-ion concentration of colloidal lead solutions. The colloidal lead solutions as prepared were also examined for the presence of CO_2 and 100-Gm. samples containing 600 mg. of colloidal lead, gave no quantitative test for CO_2 .

Lead hydroxide unites with lead to form complex lead hydroplumbites which are stable even in the dry form up to 130°C . No data are given on the solubility of these compounds so that it is not possible to calculate the lead-ion concentration of their suspensions. It would seem possible, however, that complex salts of this type are the ones which determine the lead-ion concentration of colloidal lead solutions.

SUMMARY.

The preparation and analysis of colloidal lead solutions are described.

The p_{Pb} of colloidal lead solutions was found to be between 8.74 and 10.28.

There are indications that the lead-ion concentration of colloidal lead solutions is determined by the presence of a small amount of a very insoluble lead salt but this salt could not be identified either experimentally or from data in the literature.

RESEARCH DEPARTMENT OF THE
CHEMICAL AND PHARMACEUTICAL LABORATORIES,
E. R. SQUIBB & SONS, BROOKLYN, N. Y.

¹ *Arb. Kaiser Ges. Amt.*, 26 (1907), 403.

² *Ibid.*, 26 (1907), 413.