RATE OF VOLATILITY OF CHLOROFORM FROM CHLOROFORM LINIMENT.*

BY J. W. E. HARRISSON.

The usual smile and cheerful attitude of the pharmacist is sadly missing when he is taken to task by the State Board of Pharmacy for dispensing preparations of sub-standard strength; nor does he feel any more pleased when he learns that the deficiency of chloroform in his chloroform liniment was the betraying sin. In his own mind he perceives an injustice on the part of the State Board in selecting as a test sample a preparation with such a highly volatile constituent. In many cases he will protest along this line. Others unthinkingly will advance the excuse that the preparation was of standard strength when made and they are at a loss to know why it should be below standard. A few try to place the responsibility on the manufacturer, if they have purchased the preparation.

Excuses along these lines are of little avail, but the persistent idea of unfairness led the writer to prepare a series of samples to determine the actual responsibility.

A quantity of chloroform liniment was made and bottled under various conditions in May 1922, and assayed after a period of three months—on August 10th.

Two methods of determining the chloroform were employed; the distillation method was carried out as follows:

Method 1.—Five mils of dilute sulphuric acid and twenty mils of water were placed in a small Erlenmeyer flask. Ten mils of the liniment were then pipetted into the flask keeping the tip below the surface of the acid mixture. The flask was connected with a small straight tube condenser and the chloroform distilled over slowly; stopping when the distillate began to become cloudy when collected.

The distillate was collected in what is known as a casein tube. This is similar to a small round bottle, the lower portion of which is slightly constricted and graduated in mils and tenth mils. After distillation was complete the tube was filled with water, stoppered and vigorously shaken and then centrifuged for five minutes. The resulting volume in mils of chloroform was then read off and the per cent. volume in the original calculated.

While this method was comparatively simple and rapid in many cases it required three and four determinations before check results could be obtained.

Another method was devised which proved to be as accurate as the first and having the added advantage that it was rarely necessary to repeat the estimation.

Method 2.—Ten mils of the liniment were pipetted directly into a casein tube and the tube filled with water, stoppered and vigorously shaken. One mil of a twenty-five per cent. sulphuric acid solution was then added, the tube again shaken and then centrifuged for six minutes. Of course, practically all of the camphor was carried down with the chloroform and also the liberated insoluble fatty acids from the soap. The total volume of these was read off and then a correction factor applied for the dissolved camphor and fatty acids.

Tabulated results of the examination of two lots of liniment under various conditions and time periods follow:

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LOT ONE.—ASSAYED MAY 8TH AND AUGUST 10TH.

	Anhydrous soap.	Camphor.	Chloroform Method 1.	Chloroform Method 2.	Correction figure.	Chloroform.
Original assay	3.34%	3.15%	29.00%	35.00%	5.9%	29.10%

	At room temperature daylight.		Room temperature dark.		Dark cool.	
	Chloroform Method 2.	Corrected.	Chloroform Method 2.	Corrected.	Chloroform Method 2.	Corrected.
Cork stoppered half full	31.20	25.30	33.20	27.30	....	....
Glass stoppered half full	31.20	25.30	33.00	27.10	....	....
Glass stoppered brown half full	31.20	25.30	32.50	26.60	....	....
Cork stoppered full	32.50	26.60	32.50	26.60	33.80	27.90
Glass stoppered full	31.80	25.90	32.70	26.80	33.20	27.30

LOT TWO.

	Anhydrous soap.	Camphor.	Chloroform Method 1.	Chloroform Method 2.	Correction figure.	Corrected per cent.
Original assay	3.725%	3.15%	30.00%	36.40%	6.20%	30.20%

	Glass stoppered, two ounce.			Cork stoppered.			Cork stoppered, foiled.		
Days.	Method 1.	Method 2.	Corrected. %	No. 1.	No. 2.	Corrected. %	No. 1.	No. 2.	Corrected %
2	28.50% 29.70	35.80%	29.60%	30.00%	35.90%	29.70%	30.50%	36.60%	30.40%
4	29.50	35.00	28.80	28.00 28.50	34.60	28.40	29.80	35.40	29.20
6	29.80	35.50	29.30	27.00	35.50	29.30	....	35.00	28.80
8	....	35.20	29.00	....	35 00	28.8	....	35.30	29.10
10	....	35.10	28.90	....	34.80	28.60	....	35.20	29.00

Anhydrous Soap was estimated by pipetting ten mils into a flat-bottom dish, with sand and drying at 110° C. until practically constant weight was obtained.

Camphor was determined by the use of the polariscope—a standard chloroform liniment reading +17.3° on the sugar scale.

The correction figure for Method 2 was arrived at in the following manner: Camphor having a specific gravity of 0.99, every gram of it occupied practically the same space as one mil of water; this also proved to be true when it was dissolved in chloroform. Therefore, every gram of camphor present would occupy practically the same volume in mils when dissolved in the chloroform. Allowance was made for the insoluble fatty acids that are liberated by taking into consideration their average combining power with Na_2O, and their average specific gravity. It was found that for every gram of anhydrous soap present there were liberated insoluble fatty acids which occupied a volume of 0.813 mil.

As an illustration we might take Lot Two—this contained 3.15% camphor which would occupy a total volume of 3.15 mils of the observed chloroformic layer. It also contained 3.725% anhydrous soap which would liberate fatty acids occupying a volume of 3.02 mils of the observed chloroformic layer or a total of 6.17 mils of the total observed chloroformic layer; by deduction we obtain the actual amount of chloroform.

While this method is not theoretically correct, there probably being some dissolved camphor and chloroform in the aqueous-alcoholic layer and *vice versa*, the practical application seems to be correct.

CONCLUSIONS.

Only slight decrease was noted in the chloroform content of chloroform liniment over a ten-day period and even on the three-month period, under conditions of extreme temperature, a maximum loss of only 3.8% was noted; also, quite contrary to expectations, there was no appreciable difference between the stability in glass- and cork-stoppered containers.

It seems, therefore, that the charge of unfairness in selecting such a sample as a test sample is not borne out. First, such a preparation would not normally be kept on the shelves of the average pharmacy for a period of three months. Second, if there is but little call for it the desired quantity can easily be prepared in a few moments.

It seems, therefore, that observed variations of five, and, in some cases ten per cent., cannot be justifiably excused.

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SOME PHYSICAL AND CHEMICAL PROPERTIES OF NEOROBIN.*

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I. INTRODUCTION.

Schamberg and Raiziss,[1] of the Dermatological Institute, Philadelphia, have introduced a new remedy in the treatment of psoriasis, pityriasis capitis, and some other forms of skin eruption, to which they have given the name Neorobin. Neorobin is a derivative of Chrysarobin and is made by dissolving the latter in glacial acetic acid and subsequent reduction with metallic tin.

Chrysarobin has been used quite extensively in the local treatment of psoriasis. On account of its marked staining properties, Schamberg and Raiziss have developed Neorobin which does not stain as markedly as Chrysarobin, and is more active as a reducing agent. Since Neorobin is gradually oxidized on exposure to the air, it is marketed in the form of a powder in tubes, flame-sealed under vacuum. When ready for use the powder is made up into an ointment which is then applied to the skin.

The purpose of this investigation was to devise physical and chemical tests for Neorobin which would differentiate it from Chrysarobin. It is needless to state that synthetic remedies or pharmaceuticals should be standardized or scientifically controlled whenever possible. This insures "therapeutic efficiency" and serves as a confirmatory identity test for the product. It is true that tentative assay methods of plant products and principles are often only approximate but are undoubtedly superior to empirical facts.

Most dermatologists attribute the therapeutic value of Chrysarobin in skin diseases to its reducing properties. As Neorobin has proved to be more active clinically than Chrysarobin, we have attempted to determine the relative reducing

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