

4. The Permanganate Method is unsatisfactory due to its length and excessive yields.

5. The Gravimetric Method developed for the assay of the official hypophosphite salt, while not applicable to the manganese salt, is satisfactory. The method is simple and accurate.

6. The Bromine Method has been developed for assaying the official hypophosphites, and is applicable to all the official salts. The method is simple, rapid and accurate.

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## EVALUATION OF A DETERIORATION FACTOR IN LIQUID PETROLATUM.\*<sup>1</sup>

BY P. L. BURRIN, A. G. WORTON AND F. E. BIBBINS.

### INTRODUCTION.

The fact that some samples of liquid petrolatum develop peculiar odors when stored under optimum conditions, while other samples stored under the same con-

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<sup>1</sup> From the Control Laboratories, Eli Lilly and Company.

ditions do not develop these objectionable odors, led the authors to search for a method of determining this factor. Every one will agree that much progress has been made in producing and purifying mineral oils, and that the oil which is offered on the market to-day is more stable than any oil that could have been purchased a few years ago. Nevertheless, there are oils offered to-day that meet the specifications of the United States Pharmacopœia, which after standing several months on the pharmacist's shelves will display a variety of disagreeable odors and tastes. The pharmacist and pharmaceutical manufacturer indeed have a task in selecting a satisfactory oil by any rapid scientific means, which at the same time will assure a stable product over a period of long aging.

The obvious method of testing samples of liquid petrolatum by storing them at an elevated temperature for a long period of time is satisfactory, but it is time-consuming. It is not practical at all to have to wait many weeks for the results of a test, to determine the advisability of purchasing a certain lot of mineral oil.

There has never been available for pharmacists and chemists a reliable and efficient stability test for liquid petrolatum. The United States Pharmacopœia and British Pharmacopœia since the beginning of the century have required that liquid petrolatum shall not impart more than a pale brown color to a layer of concentrated sulphuric acid after heating for ten minutes at 100° C. with frequent agitation. In this test the depth of color roughly measures the amount of carbonizable substance present. These official volumes have also required that a mixture of the oil, absolute alcohol, and sodium hydroxide solution saturated with lead oxide remain colorless after having been heated at 70° C. for ten minutes. This indicates the absence of sulphur, a common impurity in inferior petroleum from certain geographical sources (1). The British Pharmacopœia has also required that liquid petrolatum when heated on platinum foil be completely volatilized and not give off acrid vapors. These tests give only a fair estimate of the quality of an oil, and are not delicate enough to differentiate anything but a grossly impure oil from a high-grade oil.

The American refineries began to refine Pennsylvania, Mid Continent and California oils when the World War cut off the supply of Russian oils (2). The American oils, being saturated hydrocarbons of the methane series, are much more stable than the Russian oils, which are hydrocarbons of the benzene series or naphthenes, and are considered as hydrogenated aromatic hydrocarbons (3). The tests of the United States Pharmacopœia and British Pharmacopœia which seemed adequate for the relatively unstable Russian oils became inadequate for the saturated paraffins of America.

#### DISCUSSION.

Schau and Nielsen in a recent paper demonstrate a method whereby the stability of an oil may be measured spectroscopically. They examined eleven samples and found them all to have an ultraviolet absorption band with a maximum at about 2730 Å. and a minimum at about 2500 Å. The amount of absorption, and therefore the height of the absorption band, was found to be proportional to the depth of color developed in the sulphuric acid test. This spectroscopic method has a great advantage over the acid test in that it gives a numerical result instead of a comparative color. Unfortunately, few laboratories have good spectroscopes and skilled men to operate them (4).

Arditti reported in 1931 that he measured the stability of paraffin oil containing no sulphur compounds by air oxidation. This was carried out by bubbling air through the hydrocarbon oil at different temperatures and measuring the change in interfacial tension between 0.02*N* sodium hydroxide and the oil to determine the amount of oxidation. No oxidation took place at 15° C., but sixteen hours at 110° C., three hours at 123° C. and one-half hour at 150° C. showed very marked changes (5).

Green and Schoetzow in 1932 proposed exposing liquid petrolatum in flint-glass bottles to sunlight and ultraviolet light for a relatively short time to measure stability (1).

#### EXPERIMENTAL.

Several attempts were made by the authors to devise a test method before a satisfactory one was found. Most of these trials gave vague or inaccurate results.

*Method No. 1.*—The first attempt to differentiate high-grade from low-grade oils consisted of a simple aging test. Nine samples in cork-stoppered bottles were placed in a hot room at 45° C. to bring about a more rapid polymerization and oxidation than occurs at normal temperatures. At the end of six months when the bottles were opened for a comparison of odors only three of the oils possessed an unmistakably detectable odor. Any further differentiation in the quality of these oils with accuracy was impossible. The results obtained by this method do not justify the time involved in carrying it out.

*Method No. 2.*—To bring about a more rapid oxidation and development of odors by which to measure the oxidation, eleven oils were introduced into bottles with tin-lined caps, and all were placed in an oven for two weeks at 80° C. When the oils had cooled they were examined for odor. The results of this test are recorded in Table I.

TABLE I.

Sample.	Odor.	Sample.	Odor.	Sample.	Odor.
A	None	E	Odor	I	Odor
B	Slight odor	F	Odor	J	Strong odor
C	Odor	G	Odor	K	Strong odor
D	Odor	H	Odor		

That aging at 80° C. is superior to aging at 45° C. in testing liquid petrolatum may readily be seen. However, this test is far from being satisfactory in that it only distinguishes between the very good oils and the very poor ones.

*Method No. 3.*—L. Sonneborn and Sons, Inc., recently submitted to the authors an accelerated method for determining resistance of liquid petrolatums to heat and light. The method consists of subjecting the oil to twenty pounds steam pressure for one hour; allowing it to cool, and finally examining it for objectionable odor. Eleven oils were subjected to this test, the results of which are given in Table II.

TABLE II.

Sample.	Odor, Steam Pressure Method.	Sample.	Odor, Steam Pressure Method.	Sample.	Odor, Steam Pressure Method.
A	None	H	Slight	F	Strong
C	None or very, very slight	J	Slight	I	Strong
B	Very, very slight	E	Odor	K	Strong
D	Very slight	G	Odor		

Comparing Table I with Table II reveals that generally the effects of dry heat and that of steam on liquid petrolatums are parallel.

This method has the advantage of rapidity of performance; however, like many odor tests it is not entirely dependable because of the personal element involved.

*Method No. 4.*—The Standard Oil Co. of Indiana submitted a method for measuring colorimetrically, the quantity of peroxides developed after heating the oil for forty hours in a steam-bath at 211° F. The colorimetric reagent consists of an aqueous and acetone solution of ferrous sulphate, ammonium sulphocyanate and sulphuric acid. The color is developed when the reagent is shaken with the oil, the peroxides of which convert a portion of the ferrous ions to ferric ions which combine with the sulphocyanate ions to produce a dark red color. Three samples, B, I and J, were heated at 211° F. in a steam-bath in flasks with long side-arms to admit air for the oxidation. Sample I colored the reagent dark red after heating for twelve hours, while B and J gave no color reaction after heating seventy-three hours. Sample B was known to possess greater stability than J although the test did not signify it after seventy-three hours' heating. The authors found this method to be impractical because of the great amount of time required to carry it out.

*Method No. 5.*—Obviously a quicker and more accurate method to determine the stability of liquid petrolatums was desirable. The authors conceived the idea of measuring the peroxides which are readily developed in some of these oils after subjecting them to twenty pounds steam pressure for one hour. The ferrous sulphate and ammonium sulphocyanate reagent of the Peroxide Method was used for this purpose.

Ten oils were subjected to steam pressure, and then examined for peroxides. The results of this procedure together with those of the steam pressure method are given in Table III.

TABLE III.

Sample.	A. P. M. I.	Odor Index Steam Pressure Method.	Sample.	A. P. M. I.	Odor Index Steam Pressure Method.
A	1	1	F	6	7
B	2	2	G	7	9
C	3	3	H	8	6
D	4	4	J	9	8
E	5	5	K	10	10

The results recorded in Table III are interpreted numerically from 1 to 10. The greater the numerical index, in either the A. P. M. I. column or the odor column, the greater the amount of peroxides or the stronger the odor in a given sample, *e. g.*, sample K with an A. P. M. I. of 10 and an odor index of 10 contains the greatest amount of peroxides and also possesses the strongest odor of any of the 10 samples. A. P. M. I. is the Accelerated Peroxide Method index.

It is significant that the results of the odor tests, using both dry heat and steam, very closely parallel the Accelerated Peroxide Method in measuring the stability of liquid petrolatums. However, it is more significant that oils known from experience to be unstable contain the greatest amounts of peroxides.

## REAGENTS.

Solution A is made by dissolving 10 Gm. of ferrous sulphate in 500 cc. of distilled water to which has been added 10 cc. of concentrated sulphuric acid and 1 Gm. of potassium sulphocyanate. (Use glassware cleaned with chromic acid and be certain to use uneffloresced crystals of ferrous sulphate, and sulphocyanate.) After the ferrous sulphate has dissolved add 1000 cc. of commercial acetone. Filter the acetone if taken from a can to insure against contamination with rust. The resulting solution is gently refluxed on a steam-bath in the presence of clean iron wire, and it is protected from oxygen by introducing a stream of nitrogen or carbon dioxide

into the top of the refluxing condenser. Be certain the iron wire has no minute rust spots. If doubtful get new wire or rub down the questionable wire with sandpaper. Use a cork covered with heavy tinfoil between the flask and condenser while refluxing. Protect this reagent from air by keeping the containers filled with carbon dioxide or nitrogen. The *colorless solution* is stored in sealed, hard glass bottles containing a piece of clean iron wire. It is well to rinse the bottle with a small amount of the reagent before filling.

Caution should be used in handling the sealed bottles of test solution A, and the testing solution, since considerable pressure develops in storage. It is recommended that stored bottles be not more than one-half to two-thirds full.

Solution B is made by dissolving 10 Gm. of potassium sulphocyanate in 500 cc. of distilled water.

The testing solution consists of three volumes of solution A and one volume of solution B. Store in a hard glass bottle containing a small piece of clean iron wire. Here again, do not allow the solution to come in contact with the air. This solution is ready to use when it is *colorless* or possesses a slate-gray cast. Oftentimes the solution is tinted when first mixed but becomes colorless upon standing for a few hours.

#### TEST METHOD.

Add 100 cc. of the oil to be tested to a screw-capped, wide-mouth, 8-ounce jar with the entire paper liner removed from the cap. Place the jar in an autoclave after making certain that the screw cap is adjusted very loosely so that steam may enter the bottle. Adjust the steam pressure to twenty pounds, maintaining it for one hour, then remove the sample from the autoclave and allow it to cool. Wipe the moisture from the inside of the cap. Add 10 cc. of the sample to a 10-cc. graduated test-tube, then pipette in 5 cc. of the colorless *testing solution*. (Be certain to replace the air in the test-tube and in the bottle of testing solution with carbon dioxide or nitrogen.) Tightly stopper with a new cork and shake for thirty seconds, then allow the aqueous layer to separate. If the aqueous layer is colorless, the oil contains no peroxides. A pink or red color in the aqueous layer shows the presence of peroxides. A control of 10 cc. of liquid petrolatum and 5 cc. of the colorless testing solution should always be set up.

#### SUMMARY.

It may be said that peroxides are formed when deterioration takes place in liquid petrolatum. It may also be said that subjecting liquid petrolatum to twenty pounds pressure under steam for one hour ages it immediately, and develops peroxides that would ultimately be developed upon long aging.

Furthermore; it may be said that following the treatment with steam, an odor from the oil roughly indicates the presence of peroxides and that the ferrous sulphate and sulphocyanate testing solution of the Accelerated Peroxide Method very delicately detects the presence of peroxides.

Finally, oils intended for medicinal purposes, which can be made to develop large amounts of peroxides readily, will develop a disagreeable odor and taste when stored on the pharmacist's shelves. The rapidity of this normal deterioration is indicated roughly by the amount of peroxides formed.

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