

tion period after packing as specified in the U. S. P. X type processes A, B and C for fluidextracts. In the present tests, the results with 19 hours of percolation were equally as good as with 91 hours of combined maceration and percolation. This saving of time is of importance. J. U. Lloyd (18) found that percolation without maceration was best for the preparation of fluidextract of *cimicifuga*. It remains to be seen whether maceration in connection with percolation is important for other drugs. Probably the most logical way for the U. S. Pharmacopœial Revision Committee to handle this problem would be to introduce a type process for percolation without any maceration either before or after packing. This type process could be specified for only those drugs which are found from time to time to be extracted equally as rapidly and completely without maceration as with maceration.

SUMMARY.

Percolation experiments indicate that maceration before or after packing is of no advantage in promoting more rapid extraction of powdered belladonna root. When the amount of moistening liquid is not kept down to a low proportion there is a decrease in rate of extraction. No advantage is apparent in (a) vacuum maceration, or (b) preliminary maceration with water alone, with subsequent addition of alcohol.

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PHYTOCHEMICAL NOTES.*

NO. 113. AN UNUSUAL PEPPERMINT OIL.

BY SISTER M. FRANCIS XAVIER.

As a preliminary to the study of a number of *Mentha* materials, largely hybrids of which only small amounts were available, a lot of about 370 cc. of peppermint oil.

* From the Laboratory of Edward Kremers.

1930, was examined. The oil had been distilled by A. J. Schwarz and E. Baillie, August 11, 1930, from material harvested from the strain of *Mentha piperita* L. which has been raised in the Pharmaceutical Garden of the Wisconsin Pharmaceutical Experiment Station for a number of years under the direction of Professor W. O. Richtmann.

In October 1931, the oil had acquired a decided orange tint, was cloudy and had deposited a resinous sediment. Nevertheless, the odor was still pleasant though penetrating. After the physical and chemical constants had been determined, the bulk of the oil was rectified by steam distillation; 307.8 Gm. yielded 269.8 Gm. of practically colorless rectified oil, or a yield of 87.6 per cent. The aqueous distillate, approximately three liters, was twice cohobated, yielding 6.7 cc. and 4.0 cc., respectively, of oil. Added to the original rectified oil, the total amounts to 279.62 Gm. or 90.8 per cent. There remained, therefore, 9.2 per cent of non-volatile resinous material in the distillation flask. The acid value of this resin, recovered from the dried ethereal solution, was found to be 3.1, 2.6 and 2.7, respectively, in three determinations. So far as determined, the physical and chemical constants of the three oils are herewith tabulated:

	Crude Oil.	Rectified Oil.	First Cohobate.
d	0.9620 at 25°	0.9145 at 27°	0.9179 at 25° (1)
n_{D25}°	1.4721	1.4700	
α_D in 100-mm. tube	-32°	-9.42°	
Acid value	0.6	..	
Ester value	23.5 and 22.4	28.2	
Percentage ester	8.5% and 8%	10.1%	
Combined menthol	6.39%	7.8%	
Total menthol	55.40%	45.3%	
Free menthol	49.01%	37.5%	

Inasmuch as the U. S. P. states that the density of the official oil may vary between 0.896 and 0.908 at 25°, the oil must be regarded as an unusual product. Letters were, therefore, sent to the A. M. Todd Company of Kalamazoo, Mich., and to Fritzsche Bros. of N. Y. City inviting their comments. The Michigan distillers asked for a sample of the oil which was sent. The replies of both firms are herewith quoted with running comments in the form of foot-notes. To the data reported by the A. M. Todd Company the U. S. P. requirements were added in the table to admit of ready comparison.

"We do not think the sample is true *Mentha piperita*, as we know it, and its odor strongly suggests to us some type of horsemint (2). It resembles to some extent oils raised in Oregon and Washington from *Mentha piperita* but the constants are quite different than anything purporting to be Oil of *Mentha piperita* we have ever examined. We assayed a part of the sample you sent to us and below we give you both the analysis of your own oil and an average analysis of 1930 crop Peppermint raised in Michigan:

	Your Sample.	Average 1930 Crop.	U. S. P. Requirement.
Optical rotation	-7.62/25°	-25.50/25°	Varies between -23° and -33°/25°
Specific gravity	0.9166/25°	0.9001/25°	0.896 to 0.908/25°
Solubility	Insoluble in 70% alcohol Soluble in 1.1 vol. 80% alcohol	3 vol. 70% alcohol 4 vol. 70% alcohol	Soluble in 4 vol. 70% alc. showing not more than a slight opalescence and no separation of oil globules

Ester	10.72%	7.8%	Not less than 5%
Total menthol	41.65%	52.7%	Not less than 50%
Refractive index	1.4705/20°	1.4620/20°	1.4600 to 1.4710/20° C.

"The temperature at which the Optical Constants have been taken is indicated. You will note a difference of about two points (0.002) in the Specific Gravity you quote, 0.9145/27°, and the Specific Gravity our laboratory indicates (3). In checking Gravity in our laboratory a pycnometer is used and a correction of 0.00075 is calculated per 1° C. in temperature. Refractive Index we find to be a dependable Constant and it seldom, even on very weedy (4) Peppermint, runs as high as 1.4630/20°. I think we have never seen a sample purporting to be Oil of Peppermint with as high a Refractive Index as the sample you submitted nor as low Optical Rotation. If the oil is true *Mentha piperita*, it is most abnormal in all respects."

Fritzche Brothers returned two opinions: the first from the Clifton Chemical Laboratory, Clifton, N. J.; the second from the Chemical Laboratory of Schimmel & Co., Milititz b. Leipzig, Germany. Both are herewith quoted:

"The Peppermint Oil to which Prof. Kremers refers appears to be quite an unusual product. While the oils of 1930 generally have been higher in density than in former years, *i. e.*, 0.900 to 0.904, we never had any above 0.905.

"The keeping quality was very good; three samples from different sources showed a rise in density of only one point in the third decimal in each case after one year's standing."

"Wir bestaetigen Ihnen den Empfang Ihres Schreibens vom 6. d.M. und haben auf die Ausfuehrungen von Herrn Prof. Kremers zu bemerken, dass wir in den letzten drei Jahren an amerikanischem Pfefferminzoel spezifische Gewichte bis zu 0.905 (25°/25°) beobachtet haben, das will aber bei der verhaeltnismaessig geringen Anzahl von Oelen, die wir untersucht haben, nicht viel besagen und schliesst keineswegs aus, dass auch hoehere spezifische Gewichte vorgekommen sind. Jedenfalls halten wir ein spez. Gewicht von 0,911, wie es Herr Prof. Kremers an einem von ihm selbst destillierten Oel festgestellt hat, nicht fuer zu hoch, da nach den vorliegenden Beobachtungen bei amerikanischem Pfefferminzoel tatsaechlich spezifische Gewichte bis zu 0,915 und darueber vorkommen. Dass der von der U. S. Ph. angegebene obere Grenzwert von 0,908 zu niedrig ist, haben wir bereits bei Besprechung des amerikanischen Arzneibuchs erwaeht (Report 1926, 139) und gehen heute sogar noch einen Schritt weiter, indem wir als obere Grenze nicht 0,910 sondern 0.915 vorschlagen.

"Die Zunahme, die das spezifische Gewicht des in Rede stehenden Oels innerhalb Jahresfrist erfahren hat (von 0.911 auf 0,962), ist allerdings ziemlich gross und laesst auf starke Verharzung schliessen, die ja auch in dem hohen Rektifikationsrueckstand (12%) zum Ausdruck kommt. So starke Verharzungen kommen bei Pfefferminzoel besonders dann vor, wenn das verarbeitete Kraut sehr frisch gewesen ist, weil in diesem Fall leicht verharzende Bestandteile in das Oel hineingelangen, die bei vorherigem Trocknen des Krauts durch den Sauerstoff der Luft schnell in nicht fluechtige Harze ueberguehrt und dadurch unschaedlich gemacht werden (5). Es soll damit nicht ohne weiteres behauptet werden, dass dies hier der Grund ist, vielmehr kann die Verharzung auch eine reine Zufallerscheinung sein, fuer die jede naechere Erklaerung fehlt, denn es ist ja bekannt, dass unter sonst gleichen Bedingungen das eine Oel groessere Neigung zum Verharzen zeigt als das andere, und das wird sich dann im Verlauf eines Jahres immerhin schon recht deutlich bemerkbar machen. Eine direkte Anomalie koennen wir selbst in einer starken Verharzung nicht erblicken, und ebensowenig darin, dass das spezifische Gewicht nach der Rektifikation des Oels hoeher bleibt als es urspruenglich gewesen ist, denn die Verharzungsprodukte sind natuerlich z. T. fluechtig und machen dann begreiflicherweise das Oel schwerer (5)."

In order to acquire a somewhat better insight into the nature of this unusual oil, 130 cc. of the rectified product were saponified and the saponified oil distilled with steam. The oily distillate (116 cc.) was collected in fractions, the volumes and densities of which are herewith recorded:

Fraction.	Volume.	d_{22}° .
I	60 cc.	0.9060
II	9 cc.	0.9174
III	47 cc.	0.9112

Thus it becomes apparent that little more than one-half of the saponified oil has a density within the specific gravity limits of the Pharmacopœia. Subjected to fractional distillation, the bulked rectified oil yielded the following results:

Fraction.	Volume.	$d_{23.5}^{\circ}$.
-165°	1.0 cc.
165-185°	1.2 cc.	0.7646
185-200°	13.0 cc.	0.9119
200-220°	63.0 cc.	0.9171
220-240°	15.0 cc.	0.9144
Residue	12.0 cc.

Again it will be seen that the three larger fractions of the saponified (!) oil have densities greater than those of the pharmacopœial limits.

Fraction 200° to 220°, when placed in a freezing mixture, yielded crystals of menthol. Acetylation revealed the presence of 97.8% alcohol computed as menthol.

The absence of thymol and carvacrol has already been pointed out. The quantitative tests for pulegone likewise gave negative results (6).

This unusual oil shows once more how difficult it is to fix standards for volatile oils that will satisfy every one, even though the oil be a rectified product. Had the oil been of lighter density than the official lower limit, such a shortcoming could be corrected, even though with a loss, by the removal of some of the lower fractions. However, inasmuch as the density is too high, a corresponding correction might have involved a loss of menthol and menthol ester, unless the solubility tests reported by Todd indicate the presence of sesquiterpenes that could be removed. Should the peppermint grower find that a large share of his crop yields such an oil as here reported, about the only thing he can do under the present U. S. P standard is to blend it with other oils that are relatively light.

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(1) The first cohobated oil had separated into two portions: one floated on the aqueous distillate; the other was heavier than water. The latter was discarded after it had been ascertained by means of the Flueckiger test, that it contained neither thymol nor carvacrol.

(2) As already stated, the oil had been distilled from plants that have been under cultivation in the Pharmaceutical Garden for a number of years. Inasmuch as both horsemint and wild bergamot have been distilled repeatedly in the same still used for field operations, there was a bare possibility that contamination with the oil of either species of *Monarda* had taken place. However, this was excluded by making a Flueckiger test for thymol and carvacrol. The result was negative.

(3) Applying as correction for the difference in temperatures the factor 0.000755 (Schreiner), the Specific Gravity will be 0.91601/25°. Accordingly, the difference is only 0.00059, when comparison is made at the same temperature.

(4) Contamination with weeds is excluded, since the peppermint is cultivated in rows that are kept free from weeds. Should a single weed plant have been overlooked during the cultivation, this may be expected to have been discarded in the harvest. The Pharmaceutical

Garden has only a half acre experimental field of peppermint, hence, both cultivation and harvest are under rigid control.

(5) This explains satisfactorily the large amount of resin resulting upon rectification but does not account for the unusually high density of the rectified oil.

(6) Gildemeister, "Die aeth. Oele" (3rd ed.), 1, page 560.

THE CHEMISTRY OF HEPTANE AND ITS SOLUTIONS.*¹

No. 6. THE SOLUBILITY OF THE HALOGENS IN HEPTANE.

BY JOSEPH SEMB.

The heptane used was that prepared from some of the by-products obtained in the purification of hydrocarbon from Jeffrey Pine oil placed at the disposal of this laboratory in 1927 by the Ethyl Gas Corporation (1). The material employed (2) was first shaken with concd. sulphuric acid until no more charring occurred (loss 3.0 per cent). Next the oil was shaken with fuming sulphuric acid and allowed to stand over night. After that it was shaken successively with water, also with aqueous solutions of sodium carbonate, sodium hydroxide and potassium permanganate. Finally, it was dried with calcium chloride, refluxed for several hours over metallic sodium and distilled over phosphorus pentoxide. The bulk of the oil distilled within two degrees, *viz.*

550 cc. between 96.8° and 97°.

550 cc. at 97°.

550 cc. between 97° and 97.4°, barometric pressure 743 mm. The "Vorlauf" and residue amounted to 200 cc.

The chlorine (from a cylinder) used was purified by passing it through aqueous copper sulphate, water, concd. sulphuric acid and finally through a calcium chloride tower.

The bromine used was Merck's C.P. article.

Merck's U. S. P. iodine was used without additional purification.

The dissolved halogen was determined directly with standard sodium thio-sulphate (standardized against potassium dichromate) in the case of iodine. In the case of chlorine and that of bromine, the iodine equivalent was set free by the addition of potassium iodide.

Bromine-Heptane Solution.		Iodine-Heptane Solution.	
Temp.	Wt. of 5 Cc. Aliquot.*	Temp.	Wt. of 5 Cc. Aliquot.
-78.0°	3.726 Gm.	-26.5°	3.495 Gm.
-77.0°	3.742 Gm.	0.0°	3.475 Gm.
[-51.0°	3.963 Gm.]	20.0°	3.448 Gm.
-44.5°	4.161 Gm.	34.5°	3.425 Gm.
-34.5°	4.438 Gm.	55.0°	3.395 Gm.
[-32.0°	4.137 Gm.]		
-29.0°	4.724 Gm.		
-28.0°	4.777 Gm.		
-26.5°	5.066 Gm.		

* The accompanying figure shows that the weights determined at -51° and at -32° are off.

The above values are plotted on Fig. 3.

* Scientific Section, A. Ph. A., Madison meeting, 1933.

¹ From the Laboratory of Edward Kremers.