

## ESTIMATION OF CAMPHOR IN PHARMACEUTICAL PREPARATIONS

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VARIOUS methods for the estimation of camphor and camphor containing preparations, both colorimetric<sup>1,2</sup> and volumetric<sup>3,4,5,6,7,8,9</sup> have been proposed, but no method is known which is uniformly applicable to all the pharmaceutical preparations containing camphor. Castiglioni<sup>1</sup> has suggested that when camphor is heated in ethanolic solution with furfural or benzaldehyde and sulphuric acid, a violet colour or bright red colour respectively, is produced which can be used for the determination of the amount of camphor present. This method may be applicable to camphor, and spirit of camphor but in liniment of turpentine the oil of turpentine interferes with the colour production. The same is true of the method advocated for camphor by Mitchell<sup>2</sup>, wherein when camphor is heated with 2:4-dinitrophenylhydrazine reagent and hydrochloric acid and cooled, a wine-red colour is produced on the addition of ethanolic solution of potassium hydroxide.

The chemical methods are similar to those employed for the estimation of carbonyl compounds using 2:4-dinitrophenylhydrazine or hydroxylamine hydrochloride reagent. The method with the former reagent is mostly gravimetric<sup>3,4,5</sup> while the latter reagent can be used for both gravimetric<sup>6</sup> as well as volumetric<sup>5,7</sup> estimations.

In the B.P. 1953 method<sup>3</sup> the 2:4-dinitrophenylhydrazine reagent is refluxed with camphor and the 2:4-dinitrophenylhydrazone which is formed is weighed. This method gives results which are too low<sup>5</sup> owing to the decomposition of dinitrophenylhydrazone by heat, during refluxing. In the N.F. IX method<sup>8</sup> the over-heating is avoided by using a pressure-heating method, which is tedious and risky, though Ozger<sup>5</sup> finds the results to be more accurate.

In the present investigation, when the B.P. 1953 method<sup>3</sup> was used to estimate camphor in liniment of turpentine, the precipitate of 2:4-dinitrophenylhydrazone could not be separated since it remained dissolved in turpentine-oil. Attempts to remove the turpentine oil by steam-distillation resulted in a sticky mass which could not be properly washed and dried. Besides the above method, Goldstein and Reindollar<sup>9</sup> have suggested a method for the estimation of camphor, on the lines recommended by the N.F. IX<sup>10</sup>, for the assay of spearmint spirit. In this method, the volume of the separated oily layer is read after the addition of acid calcium chloride solution and a known volume of kerosene. But this method is not suitable for liniment of turpentine which contains turpentine oil in addition to camphor.

In the present investigations, successful attempts have been made to estimate camphor volumetrically in pharmaceutical preparations on the

lines suggested by Ozger<sup>5</sup> and Wolstadt<sup>7</sup>, using hydroxylamine hydrochloride. The camphor or its preparation is refluxed with hydroxylamine hydrochloride reagent in ethanol 90 per cent. for 4 hours in the presence of sodium bicarbonate. The reaction mixture is cooled and the condenser is washed with 20 ml. of light petroleum (boiling point 50° to 60°) which also aids a sharp end-point during titration. The mixture is then titrated using dimethyl yellow as indicator, with standard hydrochloric acid which neutralises the excess of sodium bicarbonate and converts the unreacted hydroxylamine to hydroxylamine hydrochloride. The solution is then titrated with standard potassium hydroxide solution using phenolphthalein as an indicator, which determined the unreacted hydroxylamine hydrochloride. A simultaneous blank experiment is conducted and the difference in the titrations between the blank and the sample gives the amount of hydroxylamine hydrochloride reacted with camphor which is calculated from the factor given in the experimental part.

In order to test the suitability of this method for camphor-containing pharmaceutical preparations, a 5 per cent. solution of camphor was made in steam distilled turpentine oil and the camphor estimated by the above method. The analysis of other pharmaceutical preparations was made after obtaining satisfactory results in this estimation.

## EXPERIMENTAL

### *Reagents*

*Ethanol 95 per cent. (aldehyde free).* 2.5 g. of lead acetate was dissolved in 5 ml. of water and the solution was added to 100 ml. of ethanol 95 per cent. contained in a glass stoppered bottle. The whole mixture was shaken thoroughly. 5 g. of potassium hydroxide was dissolved in 25 ml. of warm ethanol. The solution was cooled and added slowly to the ethanolic solution of lead acetate. After one hour, the mixture was shaken thoroughly and allowed to stand overnight. The ethanol was recovered by distillation.

*Hydroxylamine hydrochloride solution.* 4 g. of hydroxylamine hydrochloride was dissolved in ethanol 90 per cent. (aldehyde free) to make 100 ml.

Sodium Bicarbonate of B.P. quality.

*Turpentine oil, steam distilled.* 26.5 g. of Sodium Hydroxide B.P. was dissolved in 500 ml. of distilled water. This solution was mixed with 500 ml. of turpentine oil and about three-fourths of the oil collected by steam distillation. The oily portion was separated from the water, dried by shaking with anhydrous calcium chloride and filtered.

## ESTIMATION OF CAMPHOR

*Camphor in oil of turpentine.* 5 g. of camphor accurately weighed was dissolved in oil of turpentine (steam-distilled) to make 100 ml. 5 ml. of this camphor solution was refluxed for 4 hours with 20 ml. of ethanol 95 per cent. (aldehyde free), 10 ml. of hydroxylamine hydrochloride reagent and 0.3 g. of sodium bicarbonate, cooled and the condenser was

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rinsed with 20 ml. of light petroleum (boiling point 50° to 60° C.) into the flask. The mixture was titrated with 0.2N hydrochloric acid using dimethyl yellow as an indicator. The control was also adjusted to the same tint. Both solutions were then titrated to pink colour with 0.2N potassium hydroxide solution using phenolphthalein as an indicator. The amount of camphor was calculated from the difference in the volume of 0.2N potassium hydroxide used in the two titrations. Each ml. of 0.2N potassium hydroxide is equivalent to 0.0304 g. of camphor. (In the control experiment 5 ml. of steam distilled turpentine oil was added before refluxing.) (Table I.)

TABLE I  
RECOVERY OF CAMPHOR FROM OIL  
OF TURPENTINE

Experimental per cent. of camphor w/v	Theoretical per cent. w/v
4.92	5.00
4.89	5.00
4.98	5.00

### *Camphor*

The assay was carried out as described under camphor in turpentine oil, using 0.2 g. of camphor in place of 5 ml. of camphor in oil solution. (Table II.)

TABLE II  
RECOVERY OF CAMPHOR

Amount of camphor taken	Experimental per cent. of camphor w/w	B.P. Standard
0.279 g.	98.07	Not less than 96 per cent. do. do.
0.3207 g.	99.00	
0.177 g.	98.00	

### *Spirit of Camphor*

The assay was carried out as described under camphor in turpentine oil, using 2 ml. of spirit of camphor in place of 5 ml. of camphor in oil solution. (Table III.)

TABLE III  
RECOVERY OF CAMPHOR FROM SPIRIT  
OF CAMPHOR

Experimental per cent. of camphor w/v	Theoretical per cent. w/v
10.03	10.00
9.88	10.00
9.95	10.00

### *Liniment of Camphor*

About 1 g. of liniment of camphor, accurately weighed, was refluxed with 30 ml. of ethanol, 95 per cent. (aldehyde free), 10 ml. of hydroxylamine hydrochloride reagent and 0.3 g. of sodium bicarbonate. The assay was completed as described under camphor in turpentine oil commencing at the words, "Cooled and the condenser was rinsed with 20 ml. of light petroleum into the flask. . . ." (In the control experiment 1 g. of arachis oil was added before refluxing.) (Table IV.)

### *Liniment of Turpentine*

About 50 g. of liniment of turpentine, accurately weighed, was diluted with 50 ml. of distilled water, cooled and acidified with dilute sulphuric acid, using solution of methyl orange as indicator. The mixture was distilled in steam and the distillate was collected in a separator, till all the volatile matter was distilled. The aqueous portion of the distillate was separated out and the oily layer was transferred to a 250 ml. measuring

flask. The condenser and the separator were rinsed each with 50 ml. of ethanol 95 per cent. (aldehyde free) into the same measuring flask. The aqueous portion was extracted with 30 ml. of solvent ether and the ethereal extract was transferred into the measuring flask. The volume

was adjusted to 250 ml. with sufficient quantity of ethanol 95 per cent. (aldehyde free). 20 ml. of this solution was refluxed with 10 ml. of hydroxylamine hydrochloride solution and 0.3 g. of sodium bicarbonate. The assay was completed as described under camphor in turpentine oil, commencing at the words, "cooled and the condenser was rinsed with 20 ml. of light petroleum into the

TABLE IV  
RECOVERY OF CAMPHOR FROM LINIMENT OF CAMPHOR

Amount of preparation taken	Experimental per cent. of camphor w/w	Theoretical per cent. w/w
1.085 g.	19.2	20.0
1.285 g.	19.6	20.0
1.026 g.	19.7	20.0

TABLE V  
RECOVERY OF CAMPHOR FROM LINIMENT OF TURPENTINE

Amount of preparation taken	Experimental per cent. of camphor w/v	Theoretical per cent. w/v
44.695 g.	4.95	5.0
45.857 g.	4.90	5.0
45.453 g.	4.92	5.0

flask. . . ." (In the control experiment, 2.5 ml. of steam-distilled turpentine oil was added before refluxing.) (Table V.)

*Ammoniated Liniment of Camphor*

20 ml. of ammoniated liniment of camphor was mixed with 30 ml. of turpentine oil steam distilled and the mixture diluted with 50 ml. of distilled water. The assay was completed as described under Liniment of Turpentine, commencing at the words, "acidified with dilute sulphuric acid, using solution of methyl orange. . . ." (In the control experiment, 2.5 ml. of steam distilled turpentine oil was added.) (Table VI.)

TABLE VI  
RECOVERY OF CAMPHOR FROM AMMONIATED LINIMENT OF CAMPHOR

Experimental per cent. of camphor w/v	Theoretical per cent. w/v
12.26	12.5
12.16	12.5
12.35	12.5

TABLE VII  
RECOVERY OF CAMPHOR FROM LINIMENT OF SOAP

Experimental per cent. of camphor w/v	Theoretical per cent. w/v
3.88	4.0
3.87	4.0
3.95	4.0

*Liniment of Soap*

50 ml. of liniment of soap was mixed with 30 ml. of turpentine oil (steam distilled) and the mixture diluted with 50 ml. of distilled water. The assay was completed as described under Liniment of Turpentine, commencing at the words, "acidified with dilute sulphuric acid, using solution of methyl orange. . . ." (In the control experiment, 2.5 ml. of turpentine oil, steam distilled and 0.06 ml. of oil of rosemary were added.) (Table VII.)

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### SUMMARY

1. A volumetric method has been described for the estimation of camphor in various pharmaceutical preparations. This consists of reacting the preparation with an ethanolic solution of hydroxylamine hydrochloride in the presence of sodium bicarbonate and titrating the unreacted hydroxylamine hydrochloride with 0.2N hydrochloric acid and 0.2N potassium hydroxide, using dimethyl yellow and phenolphthalein respectively as indicators. In all the estimations a control experiment is necessary.

2. All seven estimations by this method give results within 96 per cent. to 102 per cent.

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