The Manufacture of Thymol from Ajowan

By J. V. Lakhani, J. J. Sudborough, and H. E. Watson.

"*Carum copticum*, also known in India as Ajowan, Juvani, Ajmo, Chochara, Owa, Omam, Omu is a herbaceous plant cultivated throughout India, especially in Bengal, and also grown in Egypt, Persia, and Afghanistan. In India it is sown in October to November in ridges, the seed being dibbled every six inches. Strong manures are deleterious, but a liberal supply of water is necessary. The aromatic fruits are much in request for admixture in curries and in *pan supari*, and are used by Indian physicians for various stomach troubles and skin diseases. They are believed to be antispasmodic, stimulant, tonic and carminative. The oil is given in cases of colic and cholera." (Watt's Dictionary of Economic Products, Vol. *2*, 198.)

For many years appreciable quantities of Ajowan seed have been exported from India. Table I gives the amounts of these exports for the years 1911-1919 with the values of the exports and the average price per cwt.

TABLE I.

Exports of Ajowan Seed.

Nearly 97 per cent from Bombay and balance from Calcutta.

Year	1911-12	1912-13	1913-14	1914-15	1915-16	1916-17	1917-18	1918-19
Total quantity exported in cwts.	15515	21650	9784	7368*	13062	11093	3090	1917
Value of the seed exported in £. ...	4583	6135	2983	2736	4871	4304	2765	2102
Rate per cwt. in shillings.	5·9	5·7	6·1	7·4	7·4	7·8	13·9	22·0
Quantity exported to Germany in cwts. ...	14210	19058	6990	6095	about 25% to the United Kingdom			
Percentage of total received by Germany ...	91·6	88·0	71·5	82·7	...	...	...	

*First three months 6164 cwt. of which 98 per cent. went to Germany (Indian Trade J., 1915, *37*, 411). In 1914-15 the United Kingdom took 382 cwt and in previous years practically nil.

From these figures it is clear that up to 1914 the bulk of the seed was received by Germany, where it was distilled for the production of thymol.

Within recent years thymol has been shown to be of great value in the treatment of hook-worm disease, and appears to be far more efficient than worm seed oil (*Chenopodium ambrosioides*), which has been recommended as a substitute.

The aqueous solution of thymol is an excellent mouth wash, and thymol is a constituent of certain tooth pastes. A list of suggested medicinal uses for thymol is given on p. 80.

There are other sources from which thymol can be obtained, but most of these, with the exception of Spanish thyme oil, have not been worked up to any appreciable extent. (cf. p. 74)

In 1919 a statement was made that a German chemist had succeeded in synthesising thymol and could put it on the market at 6 shillings a pound. Very little of this synthetic product appears to have been manufactured, as the London market price in October 1920 was 45 shillings per pound. Two synthetic processes have also been worked out in America. These are described on p. 78.

Price of Thymol.

Owing to the keen competition between the German thymol manufacturers and extensive price cutting, particularly by a large firm in Hamburg, the price of thymol for some years preceding the war bore little relation to the price of seed or the cost of manufacture. For instance, in 1911 the price of the seed in Germany was 8 sh. per cwt. Assuming the high figure of 1·2 per cent. for the yield of thymol (cf. p. 73), the cost of the seed required for one pound of thymol is 6 sh. At the time pure thymol was selling at 5 sh. per lb., but the year before, offers had been made at 3/9 sh. although the price of seed was approximately the same. The alteration in price was due to a temporary agreement between the manufacturers in 1910. In 1912 the Hamburg firm shut down and the price rose to 5/6—6/6 sh. Even at this figure it is clear that the margin for profit must have been the barest possible and in fact, if it had not been for the by-products, the manufacture would have been carried on at a loss. These by-products are:—

(a). The residual seed after the removal of the volatile oil by steam distillation. The spent seed, dried if necessary, forms a valuable cattle fodder as it contains 15 to 17 per cent of

protein and 25 to 32 per cent of fat. Assuming that it could be sold for the same price as oil cake, the seed necessary to make one pound of thymol would realise 9 sh.

(b). The oil usually known as "Thymene", which is left after the thymol has been removed from ajowan oil. This consists mainly of a mixture of the hydrocarbons cymene and dipentene and is worth about 1/6 sh. per lb. as a low grade soap perfume.

(c) The aqueous distillate left after the oil has separated from the condensed steam. This is largely used in India under the name of omum water and is sold in the bazaars for medicinal purposes. When kept for some time small amounts of thymol crystals separate on the surface and are known as "Flowers of Ajowan". It is stated that the ajowan water was also utilised in Germany, but more probably it was redistilled to recover the thymol it contained.

In 1914 the price of thymol rose rapidly; in July it was 9 shillings in August it rose to 15, and in September to 40, but it fell in October to 30 and in November and December to 20 and 21 shillings.

The prices for the years 1915 to 1919 were:—

Years.	1915.	1916.	1917.	1918.	1919.
Price per lb. in shillings ...	23·5 to 50	30 to 45	32·5 to 50	45 to 48	28 to 42·5

and in 1920 the price has ranged from 45 to 50 shillings.

The stoppage of exports led to various attempts being made to manufacture thymol in India, but in many cases in a somewhat crude and empyrical manner. In one case to which our attention was drawn, the uncrushed seeds were distilled with water over a free fire; the fuel required for obtaining oil from 100 lbs. of seeds cost from Rs. 7—8—0 to Rs. 10 (using wood as fuel at about Rs. 8 per ton), or nearly 4 lbs. of wood for 1 lb. of steam; the ratio of steam to ajowan oil was nearly 200; and the distillation lasted 30 hours or more.

The same firm ground the seeds and then found that the fine meal when boiled with water charred and formed a hard cake at the bottom of the still.

By using a steam boiler, crushed seeds and lagged stills 1 lb. of steam can be obtained from 1/2 to 1/3 lb. of wood, and the ratio steam to oil is about 100 : 1 (p. 72).

Methods of Refining Thymol.

The Imperial Institute in 1917 gave directions for the preparation of thymol in which they recommended ether, petroleum ether or acetic acid for purposes of recrystallising. In the latter case the crystals are opaque and have to be fused and allowed to recrystallise.

In working on the small scale the excessive solubility of the thymol in solvents like alcohol and petroleum ether, indicated that on the large scale the refining would not be easy. Our attention was therefore directed towards methods of refining the crude thymol without the aid of a crystallising medium, and after preliminary experiments we found that on the small scale thymol could readily be refined by distillation with steam at about 130 to 140°C. The method we used was as follows:—

The thymol was placed in a flask provided with a cork with 3 holes. This flask was immersed in an oil bath so that the whole of the body and the greater portion of the neck was below the surface of the oil; this was accomplished by heavily weighting a wire netting which covered the flask. Before entering the flask, the steam was passed through a coil of lead tubing which was coiled round the flask and immersed in the oil. A thermometer registered the temperature of the mixture of steam and thymol vapour just as it left the flask and a second thermometer was placed in the oil which was kept at about 10°C. above the temperature of the vapour issuing from the flask. A glass condenser was used and the temperature kept at about 50° so that there was no risk of the thymol solidifying in the inner tube.

The distillate was collected in a small florentine flask and the cake of solidified thymol, which was obtained on cooling, was quite white.

In order to determine a suitable temperature at which to carry out the distillation, experiments were made in which the ratio between water and thymol in the distillate was measured for different temperatures.

The following figures were obtained by Mr. B. M. Gopalsawmy Reddy with the above apparatus except that the florentine flask was replaced by a small separating funnel, the tap of which was opened slightly so as to allow the aqueous distillate to drain away automatically into a measuring cylinder.

200 grams of thymol was used in each experiment and the distillate collected in several portions. In each of these the

water and thymol were separated and weighed. Table II shows the weight of water per unit weight of thymol in every case. It will be observed that at first the ratio is fairly constant but towards the end of the experiment it increases. This is due to the small quantity of thymol remaining in the flask and consequent incomplete saturation of the steam with its vapour. These high figures are not taken into account when calculating the mean values. The mean atmospheric pressure during the experiments was 680 mm.

TABLE II.

Weight of steam required to distil unit weight of thymol at different temperatures.

Temperature	100°		110°		120°		130°		140°	
	a	b	a	b	a	b	a	b	a	b
Fraction 1 ...	14·8	15·1	8·79	9·00	5·56	5·66	3·47	3·43	2·09	2·31
2 ...	15·0	15·2	8·91	8·94	5·46	5·45	3·44	3·45	2·15	2·31
3 ...	17·1	15·5	8·75	8·74	5·48	5·50	3·52	3·50	2·22	2·29
4 ...	30·9	16·0	9·15	9·27	5·52	5·50	3·54	4·00	2·28	2·42
5	...	15·9	9·55	9·50	12·17	5·85	3·80	4·07	3·00	3·80
6 ...	...	16·9	...	12·0	...	...	...	...	...	...
Mean ratio Thymol water.	1 : 15·1		1 : 8·96		1 : 5·52		1 : 3·48		1 : 2·28	
Calculated ratio ...	1 : 13·0		1 : 7·65		1 : 4·50		1 : 2·70		1 : 1·77	

An increase of 10° at temperatures between 100 and 140°. produces an increase of 53 to 68 per cent in the amount of thymol carried over by one part by weight of steam.

In the last line of the table the ratio of thymol to water has been calculated approximately by assuming that the vapour pressure of thymol at 109°C is 10mm. and that the vapour pressure curve is of similar shape to those of *m*-chloraniline and ethyl salicylate, which boil at temperatures not far from that of thymol. (Cf. Rechenberg, Gewinnung u. Trennung der aetherischen Oele. p. 362.) The agreement is poor. Possibly the figure for the vapour pressure of thymol, which is an old determination, is incorrect.

PRODUCTION OF THYMOL ON SEMI-COMMERCIAL SCALE.

We next carried out experiments on a semi-commercial scale working with charges of about 300 lbs of seed.

The details to which we paid attention were :—

1. The sifitng and crushing of the seeds before distillation.
2. Distillation with steam generated in a boiler separate from the still.
3. Steam economy by lagging the still and steam pipes.
4. The separation of as much crude thymol as possible in the solid state without extraction with caustic soda and precipitation with sulphuric acid.
5. The refining of the crude thymol by distillation with steam at about 130°C.
6. The obtaining of the refined thymol in the form of large clear colourless crystals by fusing and allowing to crystallise spontaneously during slow cooling.

The following is a brief resume of the process finally adopted :—

(*a*) *Treatment of the seed.* The seed was first sifted to remove stones, dust and sand, and was then crushed between smooth rollers : these were so adjusted that each seed was crushed but the whole mass did not cake. The percentage of impurity varied from 2 to 7 per cent in different samples.

(*b*) *Distillation.* In the earlier experiments a copper tilting still of 300 lbs capacity was used and later a copper still of 1500 lbs capacity *viz.* 6'×4'. The stills were made of 1/16″ sheet copper. A perforated tray was placed at the bottom and below this was the steam inlet. The still was attached by a copper outlet pipe to a copper tube condenser and no part of the apparatus was tinned, as it was found that when the distillate came into contact with tin, the oil became quite black in colour, but when bare copper was used the colour was much paler.

(*c*) *Products of distillation.* During the earlier part of the distillation the ratio oil : steam is much higher than later on, as the by-products dipentene and cymene are much more readily volatile with steam than is thymol. Thus in the course of the first 1·5 to 2 hours 40 to 50 per cent of the total yield of oil

passes over, but this contains only about 15—17 per cent. of thymol. The rate at which the oil comes over decreases but it becomes richer in thymol and finally nearly pure thymol is obtained.

The earlier distillates were always kept separate from the later ones; as soon as a product was obtained which gave crystals of thymol on inoculation, the receiver was changed and a second fraction collected. This was done 2·5 to 3 hours after the beginning of the distillation when 45 to 47 per cent of the total yield of the oil had distilled over.

(*d*) *Treatment of the two fractions.*

I. The earlier oil fractions were shaken with 20 per cent. sodium hydroxide solution in iron drums, the two layers allowed to separate and the lower aqueous layer run off. The residual oil was shaken a second time with a relatively small amount of sodium hydroxide solution, the aqueous layer added to the original alkaline extract, and the whole was then acidified with a slight excess of sulphuric acid and allowed to stand.

A layer of brown oil collected on the surface of the acidified liquor and this rapidly set to a cake of brownish yellow crystals of thymol. This cake was broken up, the acid liquor drained away and the crystals washed several times with small quantities of water until free from acid.

II. The later fraction, when separated from the condensed water, was allowed to stand for several hours in enamelled pans about 15″ diam. when a considerable amount of thymol crystals had separated. Further quantities of crystals can be obtained by cooling to 0° or by allowing to stand for several days when part of the thymene oil evaporates. In most cases however the mother liquor from the first batch of crystals was treated in exactly the same manner as the earlier fractions *viz.*, shaking with sodium hydroxide solution to remove the thymol remaining in solution, the only difference being that more dilute —5 to 7 per cent.—sodium hydroxide was used, as otherwise an emulsion was usually obtained. The thymol liberated on acidifying with sulphuric acid readily crystallised but always contained small amounts of a high boiling oily product, which was removed as far as possible by washing and draining. This oily product was used for protecting wood against white ants.

The crystals were powdered and again washed with cold water to remove adhering oil.

In both cases it would have been easier to centrifuge the thymol crystals and wash them on the centrifuge but one was not available.

The washed crystals were placed on canvas shelves, covered with canvas and left for a day in order to dry and to get rid of last traces of oil.

(*e*) *Steam distillation of the thymol crystals.*

For this purpose a steam jacketed cast iron still of about 20 gallons capacity and provided with a copper cover fitted with baffle plates and an inlet tube for steam was utilised, 50 to 80 lbs. of the crude crystals were distilled at a charge and the distillate was condensed in a copper worm condenser 24″ in diameter, care being that the distillate ran warm at about 50° C, so that no thymol solidified in the tube. The temperature of the distillate at the top of the goose neck was 130°C. when the steam in the jacket was at 40 lbs pressure, and steam was passed at the rate of 70 lbs. per hour. At this temperature the ratio of thymol to steam was about 1 : 3·5 (cf. Table II) and the distillation of 80 lbs. of thymol took 3 to 4 hours. The colourless oily layer of thymol was removed and stirred while crystallising, so that small crystals were formed. These were spread on canvas shelves until quite dry and were then fused in clean aluminium or copper pans, and allowed to cool slowly when large clear transparent colourless crystals were obtained By this means very large and excellent crystals are formed. If there is the least tinge of yellowish colour in the fused thymol, it is advisable not to let the whole solidify, but after about 75 per cent. has solidified, to pierce two holes in the crystalline mass and run off the liquid portion. The crystals will be quite colourless and the yellow liquor which is run off, can be redistilled with steam.

In the process of recrystallising by fusion and allowing to cool slowly it is necessary to fuse every particle of solid in the dish otherwise on cooling a minute crystal adhering to the upper part of the pan will start crystallisation as soon as the liquor cools and rather small, opaque, white crystals will be formed. The liquor must be allowed to under cool, and the crystals left to form slowly by themselves.

Varieties of seed.

The fruits from the different parts of the country give different percentages of oil varying from 2·0 to 3·5. A stat ment is frequently made that the yield of oil is from 3 to 4 per cent but we have not met with seed yielding more than 3·5 per cent,

One variety of seed, which appears to grow in the Madras Presidency, gave a high yield of oil *viz.* 3·5 per cent. These seeds are thicker than the ordinary seeds and of a yellow colour.

A thin variety of seed obtained from the Punjab or Cawnpore gave about 2·07 per cent of oil.

The average yield of oil from seeds obtained in Bombay is 2·5 to 3·0 per cent.

Results of Distillations.

The following tables give details of some of the results obtained. Table III shows the progress of a distillation carried out in the smaller still. In this case the distillation was stopped at night. The oil and condensed water were weighed and the ratio of the weights is given in the last column.

Tables IV and V give results obtained when working with the larger still. Table IV shows two distillations carried out with the same batch of seed under nearly the same conditions, but in the second case a larger charge of seed was used. The result was a slight diminution in the yield, and an increase in the amount of steam required per pound of oil. Table V shows the improvement effected by using thick seed.

Table VI is a summary of the results of a number of distillations. Distillations XI—XIII show that thick seed gives a higher yield of oil than the other varieties, but as this costs from 1 to 2 rupees a maund of 80 lbs. more than the other, there is little, if any economy effected by its use.

Distillations XIV to XVII carried out with old seed (probably about a year old) show that a longer time is taken for distillation and that the yield is lower than in the case of the fresh seed. It is possible that this low yield is due to partial evaporation of the thymene oil on storage, but unfortunately the

distillate from these experiments was not kept separately, so that no determination of the actual thymol content could be made. It is interesting to note that the average ratio of oil to steam for these distillations is 0·0077 which is the figure given by Rechenberg (Gewinnung und Trennung der aetherischen Oele p. 362). This is probably the average figure obtained in Germany, showing that it is advantageous to distil the fresh seed before shipment.

Distillations XVIII to XXI were carried out with a somewhat smaller rate of steam and required more steam per pound of oil than the earlier distillations, but judging from the distillation of other materials, the difference is more than can be accounted for by the rate of steam, and is probably due mainly to the use of a different batch of seed.

Table VII shows the quantities of oil and thymol obtained from each group of distillations that was carried out. It will be noted that the oil contains from 39 to 45 per cent. of crude thymol, and this in turn yields about 85 per cent. of pure thymol, making the yield from the seed very nearly 1 per cent. The loss on purification is not due to any decomposition but to impurities adhering to the thymol crystals.

In no case do the figures include the thymol which remains in solution in the water. According to E. M. Holmes, (Perf. & Essent. Oil Record 1916, 7, 311) the solubility of the oil in cold water is 0·114 per cent. with 90 per cent. of phenols so that about 10 per cent of the total thymol is lost if the water is thrown away. Our own experiments show that under working conditions the amount of pure thymol dissolved in 100 lbs. of water is about 0·038 lb.* so that the loss would be 3·8 per cent of the total thymol. This loss can be avoided by neutralising the distillate and using it to feed the boilers, or, if other essential oils are being prepared in the same factory, by redistilling about 5 per cent of the liquor.

* This number is only approximate and will be checked later.

Table III.

Distillation of 171·5 kg. of crushed seed, not freed from dust or stones.

Time.	Interval.	Total hours.	Quantity of oil.	Total oil.	Quantity of water condensed	Total water condensed.	Mean ratio, grams oil/kg. water.
3 d Sept. 8·48 A. M.							
9 15 A. M.	0·5 hrs	0·5	0·918 kg.	0·918 kg.	9·0 kg.	·0 kg.	102·0
10·45 „	1·5 „	2·0	0·828 „	1·746 „	22·5 „	31·5 „	26·3
1·15 P. M.	2·5 „	4·5	0·515 „	2·261 „	45·0 „	76·5 „	11·4
3·15 „	2·0 „	6·5	0·237 „	2·498 „	36·0 „	112·5 „	6·6
5·30 „	2·25 „	8·75	0·192 „	2·690 „	30·6 „	143·1 „	6·2
4th Sept. 8·35 A. M.							
11·35 „	3·0 „	11·75	0·267 „	2·957 „	56·3 „	199·4 „	4·8
2·35 „	3·0 „	14·75	0·247 „	3·204 „	54·0 „	253·4 „	4·6
5·5 P. M.	2.5 ,	17·25	0·104 „	3·308 „	49 5 „	302·9 „	2·1
5th Sept. 10·35 A. M.							
12·35 „	2·0 „	19·25	0·060 „	3·368 „	57·6 „	360·5 „	1·0

0·303 kg oil recovered from second collecting vessel. Total yield of oil = 3·671 kilos equivalent to 2·14 per cent.

Mean ratio oil : water = 1·04 : 100. Average rate of steam = 18·8 kg. per hour.

Table IV.

13th July 1918.

Distillation of 1300 lbs of thick sifted seed freed from stones and dust and crushed between rollers.

Time.	Interval.	Total hours.	Oil in lbs.	Total oil in lbs.	Rate of steam lbs. per hour.
7·50 A. M.					
8·50 „	1·0 hrs.	1·0	16·5	16 5	200
11·20 „	2·5 „	3·5	6·6	23 1	„
4·20 P. M.	5·0 „	8·5	8·25	31·35	208
9·20 „	5·0 „	13·5	5·6	36·95	200
11·20 „	2·0 „	15·5	1·7	38·65	„
12 50 A. M.	1·5 „	17·0	0·5	39.15	„
1·50 „	1·0 „		nil		

Yield of oil=3·01 per cent.
Mean ratio=0·0114 lbs oil per 1 lb steam.

1st August 1918.

1500 lbs of crushed seed, freed from dust and stones.

8·30 P. M.					
9·30 „	1·0 hrs.	1·0	16·0	16·0	204
11·40 „	2·17	3·17	7·0	23·0	„
4·10 A. M.	4 5	7·67	7·0	30·0	„
9·40 „	5·5	13·17	7·25	37·25	„
1·10 P. M.	3·5	16·67	4·6	41·85	„
3·10 „	2·0	18·67	1·0	42·85	„
4·30 „	1·33	20·0	0·75	43·60	„
5·30 „			nil		

Yield of oil=2·91 per cent.
Mean ratio=0·0107 lb oil per 1 lb steam.

Table V.

Distillation of 1400 lbs. of thick seed freed from dust and stones and obtained as fresh crop. 14th August 1918.

Time.	Hours.	Total hours.	Oil in lbs.	Total oil in lbs.	Rate of steam lbs. per hour.
7·15					
9·15	2·0	2·0	20·5	20·5	160
1·45	4·0	6·0	9·0	29·5	200
6·45	5·0	11·0	9·0	38·5	„
10·45	4·0	15·0	5·6	44·1	„
1·15	2·5	17·5	2·6	46·7	„
3·15	2·0	19·5	1·5	48·2	„
4·15	1	20·5	0·25	48·45	„
			0·55 from collecting pots.	49·0	„

Yield of oil = 3·50 per cent.

Mean Ratio = 0·0122 lbs. oil per 1 lb. steam.

TABLE VI.

Statement showing the results of various distillation carried out in 1918.

Date.	No.	Remarks.	Weight of seed used.	No. of hours distillation lasted.	Total quantity of oil obtained.	Percentage yield of the oil.	Average rate of steam lbs. per hour.	Total water condensed lbs.	Mean ratio oil to steam × 1000
24th July	I	Fresh crop medium seed sifted and crushed.	1856 lbs.	...	39·0 lbs.	2·88	...	...	...
29th ,,	II	,, ,,	1300 ,,	18·0	39·5 ,,	3·04	216	3888	10·1
30th ,,	III	,, ,,	1300 ,,	17·0	39·15 ,,	3·01	202	3440	11·4
1st Aug.	IV	,, ,,	1500 ,,	20·0	43·60 ,,	2·91	204	4080	10·7
2nd Aug.	V	,, ,,	1400 ,,	20·5	41·25 ,,	2·95	220	4510	9·1
5th Aug.	VI	,, ,,	1430 ,,	19·75	39·35 ,,	2·75	200	3950	10·0
6th ,,	VII	Fresh crop thin seed sifted & crushed, fresh consignment	1450 ,,	23·5	43·25 ,,	3·00	Not measured		
10th ,,	VIII	,, ,,	1300 ,,	19·0	30·95 ,,	2·38	,,		
11th ,,	IX	,, ,,	1400 ,,	19·5	42·0 ,,	3·0	,,		
13th ,,	X	,, ,,	1300 ,,	19·0	41·0 ,,	3·15	206	3914	10·5
14th ,,	XI	Fresh crop, thick seed sifted and crushed.	1400 ,,	20·5	49·0 ,,	3·5	196	4020	12·2
16th ,,	XII	,, ,,	1300 ,,	20·0	43·0 ,,	3·30	185	3700	11·6
19th ,,	XIII	,, ,,	1400 ,,	23·5	43·6 ,,	3·30	...	...	...
20th ,,	XIV	Old crop thick seed sifted and crushed.	1450 ,,	25·0	38·0 ,,	2·62	200	5000	7·6
21st ,,	XV	,, ,,	1500 ,,	27·0	41·63 ,,	2·80	,,	5400	7·7
23rd ,,	XVI	,, ,,	1500 ,,	24·5	38·24 ,,	2·55	,,	4900	7·8
28th ,,	XVII	,, ,,	1500 ,,	25·5	39·0 ,,	2·60	,,	5100	7·6
9th Sept	XVIII	Medium seed sifted and crushed.	1400 ,,	29·5	39·5 ,,	2·82	179	5287	7·5
13th ,,	XIX	,, ,,	1500 ,,	30·0	45·0 ,,	3·0	160	4800	9·4
14th ,,	XX	,, ,,	1500 ,,	30·5	43·0 ,,	2·87	175	5337	8·1
	XXI	,, ,,	1500 ,,	25·5	43·2 ,,	2·87	190	4844	8·9

TABLE VII.

Statement showing yields of oil, crude thymol and refined thymol.

Quantity of seed in pounds.	Yield of oil in pounds.	Percentage yield of oil.	Yield of crude thymol in pounds.	Percentage yield of crude thymol from oil.	Percentage yield of pure thymol from oil.	Yield of pure thymol from crude crystals.	Percentage yield of pure thymol from seed.	REMARKS.
32686	928·14	2·84	370·0	39·9	33·3	83·5 per cent	0·95	Fresh thick and thin and old seed.
5700	155·0	2·72	64·6	41·7	...	...	...	Medium seed
8776	254·0	2·90	110·0	43·3	...	...	...	„ „
4500	125·0	2·78	53·0	42·5	...	...	...	„ „
7100	208·0	2·93	93·5	45·0	...	...	...	„ „
26076	742·0	2·85	321·2	43·3	36·4	84·1 „	1·03	Mostly medium seed
22227	652·5	2·94	269·12	41·3	34·3	83·4 „	1·01	„ „ „
32380	943·75	2·91	370·5	39·2	34·3	87·1 „	1·00	„ „ „

The above figures do not include the thymol dissolved in the watery distillate which amounts to about 0·04 per cent on the weight of seed.

Sources of Thymol.

In considering the distillation of thymol from the fruits of Indian *Carum copticum* (Benth.) the possibility of other sources of the phenol has to be taken into consideration.

Two papers dealing with sources of thymol have been published; one by J. C. Umney in the Perf. and Essent. Oil Rec., 1914, *5*, 372 and the other in the Bull. Imp. Inst., 1914, *12*, 601. Since 1914 other sources have been examined and the following is a statement of all the sources hitherto suggested, with, as far as possible, details of yields.

1. *Carum copticum*, (Benth.) It is usually stated that the seed yields 3 to 4 per cent of oil and that the oil contains 40 to 45 per cent. of thymol. Our experiments indicate that the highest percentage is about 3·5 (Kurnool District) and that seed from North India frequently contains as little as 2·5 per cent. The percentage of thymol which can be recovered from the oil varies from 33 to 37 (cf. Table VII).

Attempts have been made to acclimatise the plant in other parts of the world, more particularly in the Seychelles and in Montserrat (Bull. Imp. Inst., 1918, *16*, 30). Although the fruits from the former appeared badly developed they gave a 9 per cent yield of oil containing 38 per cent of thymol. In Montserrat after 6 months a maximum yield of 1128 lbs. of fruits per acre was obtained and this gave 2·7 to 3·1 per cent. of oil containing 54 per cent of thymol. The average yield for 2 years was 503 lbs. per acre and varied between 360 and 1128 lbs. Only the very best lands are of use and an ample rainfall is necessary. Careful attention is required in the early stages of cultivation and the main difficulty is the cost of collecting the fruits (Taken from Report of Commissioner of agriculture for West Indies. cf. Perf. and Essent. Oil Rec., 1919, *10*, 214). Both results are better than those obtained from Indian seed, and if the yield of oil from the Seychelles seed can be maintained, the fruits would rapidly displace those grown in India.

2. *Monarda punctata*. L., The American Horsemint. An extremely interesting and detailed account of experiments on the plant has been published in Bulletin No. 372 of the U. S. Department of Agriculture (*cf.* E. M. Holmes, Perf. and Essent. Oil Rec., 1916, 7, 311). In 1910 a series of experiments

was started on cultivating the plant, and the first year 0·20 per cent of oil was obtained on distilling the leaves, the second year the yield was 0·24 per cent and the oil contained 64 per cent of phenols and by 1915 leaves were obtained giving 0·42 to 0·44 per cent. of oil containing 72 per cent. of phenols. Experiment has shown that it is better to distill the plants at once and not allow them to dry as this means loss of oil. The plant is cut about 6 inches above the ground in the flower bud stage, as the loss of phenols is very rapid as the flowering stage advances. The water which separates from the oils yields, when distilled, about one-seventh of the original amount of oil obtained from the plant and is extremely rich in phenols.

The commercial yield is 66·3 per cent. of thymol. It is estimated that 1 acre will give 12·86 lbs. of thymol the first year and 19·29 lbs in subsequent years and that replanting must take place every 5 years. The costs of cultivation are given as 23 dollars per acre the first year, 19 dollars subsequently and the profits about 16 dollars per acre.

The American Horsemint has also been cultivated in Montserrat (Perf. and Essent. Oil Rec., 1919, *10*, 242). The yields are given as follows—green growth 4416 lbs per acre, oil 57·54 c.c. per acre; thymol content 44 per cent or 80·33 oz. of thymol per acre. These yields are distinctly inferior to those given in the American Bulletin No. 372.

3. *Ocimum Viride.* (Willd.,) or the Mosquito plant (Bull. Imp. Inst., 1917, *15*, 322) is a native of West Africa but has been introduced into India, Cyprus and the West Indies. The leaves of the plant from Nigeria and Sierra Leone yield 0·35 to 1·2 per cent of oil containing 32 to 65 per cent of thymol. When grown in the Seychelles the yield of oil is about 0·5 per cent. This was valued at 5 to 6 shillings per pound in 1917.

It is possible to get 5 or 6 cuttings of the plant per annum and the yield of oil is about 38 lbs per acre.

4. *Thyme oil. Thymus vulgaris* in S. France yields an oil—thyme oil—which contains both thymol and the isomeride carvacrol, but French thyme grown in Germany and varities of Spanish thyme contain thymol and no carvacrol. (J. C. Ummey Perf. and Essent Oil Rec., 1914, *5*, 372). The yield of oil is 1·7 to 2·6 according to E. J. Parry (*ibid.* 1920, *11*, 139) At one time

the Spanish thyme oils imported into England contained carvacrol, but within recent years parcels of Spanish oil containing thymol and not carvacrol have been received and utilised for the production of thymol, and at present this is the chief source from which thymol is being manufactured in England. Oil of thyme varies in price according to the phenolic (thymol) content and in September 1920 the following were the London selling prices.

30—35 per cent phenols	9·5 shillings per pound
45—50 „ „ „	11·25 „ „ „
60 „ „ „	13·5 „ „ „

According to E. M. Holmes (Perf. and Essent. Oil Rec. 1920, *11*, 338) there are 30 species of *Thymus* growing in Spain Very few of these have been investigated in detail, but *Thymus Vulgaris*, L. which flowers in spring and *Thymus Zygis*, L. which flowers in the summer yield oils containing thymol. This latter species appears to be the one from which the Spanish oil of thyme imported into England during recent years has been distilled.

5. *Ocimum gratissimum* (Bull. Imp. Inst., 1918, *16*, 32) grows as a weed in the Seychelles. The shoots give 0·1 per cent of oil but the phenolic constituent is eugenol. A variety of the same plant which grows on the Ivory Coast (W. Africa) yields an oil with a thymol content of 44 per cent.

6. *Cunila mariana* L. is indigenous to N. America and the dry herb yields 0·7 per cent of oil containing about 40 per cent of phenols stated to be thymol. (*ibid*, 1914, *12*, 601).

7. *Saturcia thymboa* L. According to Schimmels' Report Oct. 1889, 55, this plant yields an oil containing 19 per cent of thymol.

8. *Mosla japonica*. (Maxim.) is a plant indigenous to Japan and gives 2·13 per cent. of oil containing 44 to 50 per cent of thymol. Sometimes carvacarol is found but the two phenols never occur in the same sample of oil. (Hoshino, J. Chem. Ind. Tokyo, 1919, *22*, 557, *cf.* J. S. C. I., 1919, *38*, 877 A.)

9. Many Marjoram oils contain either carvacarol or thymol. According to Umney (Perf. and Essent. Oil Rec., 1914, *5*, 372)

the oil from *Origanum hirtum* L. contains thymol only. The dry herb from Dalmatia yields 3·3 per cent of oil containing 66·6 per cent of thymol (*ibid*, 1913, *4*, 7, 41, 69 and Bull. Imp. Inst., 1914, *12*, 602). *O. floribundum* Munb. in N. Africa yields an oil which contains 25 per cent of thymol.

Carvacrol.

Carvacrol has been recommended as a substitute for thymol (Bull. Imp. Inst., 1914, *12*, 599); its antiseptic properties are nearly as powerful as those of thymol (Martindale, Perf. and Essent. Oil Rec., 1910, *1*, 266) and it yields an iodo-derivature which is 5 times as efficient as iodoform as a bactericidal reagent.

Carvacarol has been synthesised recently from cymeme (cf. Hickson "A study of the conditions essential for the commercial manufacture of carvacarol," Dissertation University of Colombia, New York, 1918. Hickson and Mekee, J. Ind. Eng. Chem., 1918, *10*, 982,) and it is claimed that it can be propuced at 60 cents per pound, using cymeme from spruce turpentine.

The following yield oils rich in carvacrol :—

Monarda fistulosa L. or wild bergamot, 52—58 per cent.

Saturcia hortensis L. 38—42 per cent.

Saturcia montana L. or white thyme, up to 65 per cent.

Origanum onites L. of Trieste, 60—85 per cent.

Origanum maru D. of Syria, 72 per cent.

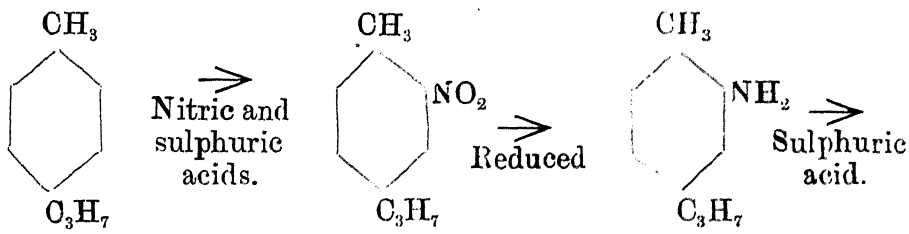
Origanum majoranoides (Willd). of Cyprus, 78 to 84 per cent.

Mosla grosserrata (Maxim) 25 per cent (J. Chem. Ind. Tokyo, 1919, *22*, 382, *cf.* J. S. C. I., 1919, *38*, 877 A.)

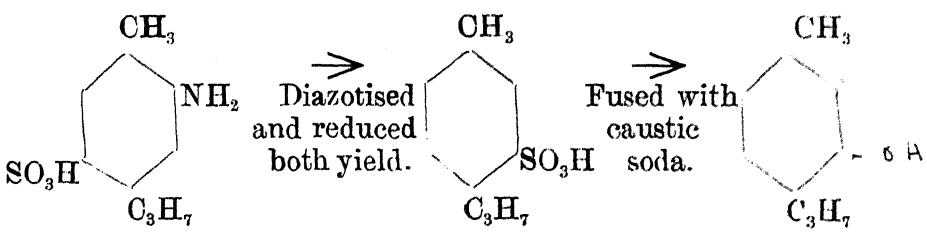
Syntheses of Thymol.

In addition to the German synthesis (*cf.* p. 60), details of which are not known, the following methods of synthetical formation have been worked out.

1. A process elaborated by M. Phillips and H. D. Gibbs (J. Ind. Eng. Chem., 1920, *12*, 733; *cf.* Perf. and Essent. Oil Rec., 1920, *11*, 335) starts with *p*-cymeme and may be represented by the following series of reactions:—



p-Cymene — 2-Nitrocymene. — Cymidine or 2-Aminocymene.

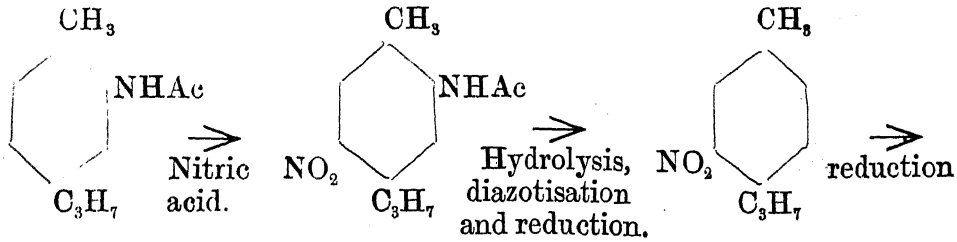


2-Aminocymene 5-sulphonic acid and the isomeric 3-sulphonic acid. — Cymene-3-sulphonic acid. — Thymol or 3-hydroxycymene.

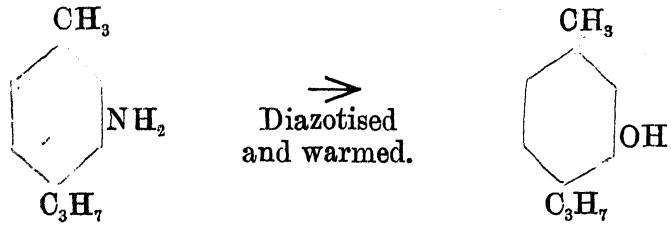
Full details are given of the isolation of *p*-cymene from the crude oil obtained from a sulphite spruce mill and also full details of the several operations depicted in the above scheme.

2. An American patent by C. E. Andrews (U. S. Patent 1306512 of 10-vi-1919; *cf.* J. S. C. I., 1919, *38*, 658 A) makes use of the same original hydrocarbon and after nitrating and reducing to cymidine converts this base into its acetyl derivative, which is then nitrated, the acetylamino group hydrolysed

and the resulting amino group eliminated by diazotisation and reduction. The 3-nitrocymene thus obtained is reduced and the amino group replaced by hydroxyl.



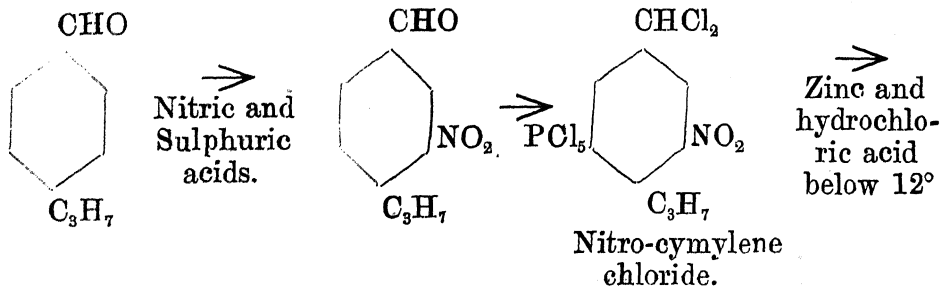
2-Acetylamino-cymene. 5-Nitro-2-acetyl-amino-cymene. 3-Nitrocymene.



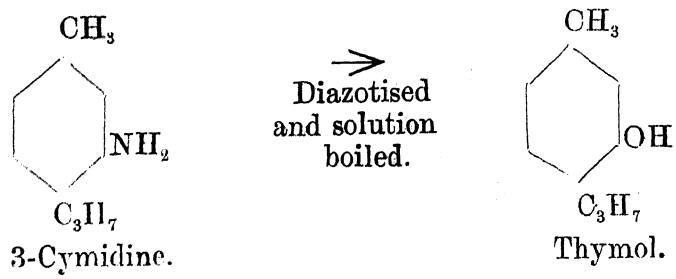
2-Aminocymene. Thymol.

Several other syntheses have been described in chemical literature, but most of these are not of technical importance.

O. Widmann (Ber., 1882, *15*, 166) synthesised thymol from cuminaldehyde by the following series of reactions:

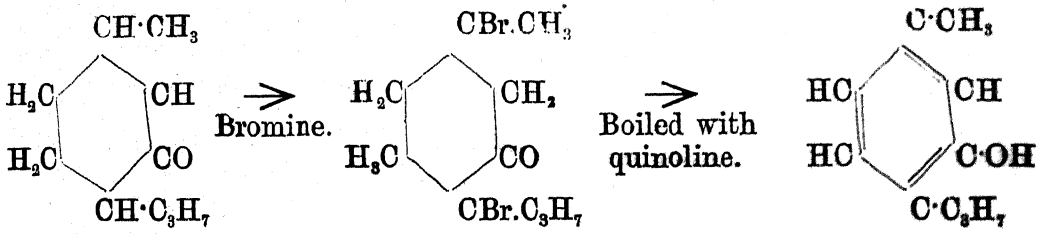


Nitro-cymylene chloride.



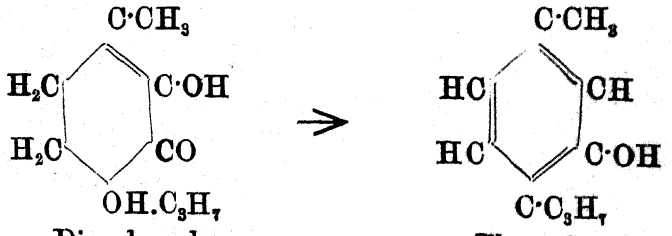
3-Cymidine. Thymol.

E. Beckmann and H. Eichelberg (Ber., 1896, *29*, 420) obtained good yields of thymol from menthone.



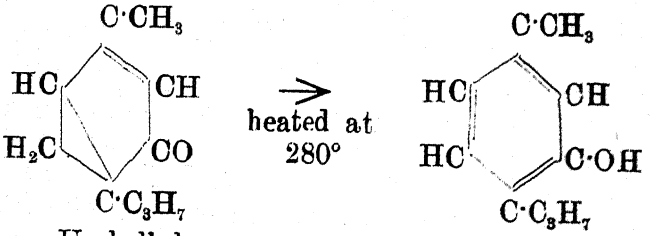
Menthone. Thymol.

F. W. Semmler and McKenzie (Ber., 1906, *39*, 1163) obtained a good yield of thymol with a little carvacrol by heating diosphenol, a constituent of Bucca camphor obtained from various species of *Barosma* in S. Africa, with concentrated hydrochloric acid at 150—180° for 2 hours.



Diosphenol. Thymol.

and finally F. W. Semmler (Ber., 1906, *41*, 3993) obtained a theosetical yield of thymol by heating umbellulone for 18 hours in sealed tubes at 280°. Umbellulone constitutes 40 per cent of the essential oil from *Umbellularia Californica*, Nutt. and can be isolated by fractional distillation.



Umbellulone. Thymol.

Uses of Thymol.

The chief characteristic of thymol is its high antiseptic and germicidal property and it is for this reason that it has taken a high place in medicine.

1. One of its chief uses is for the treatment of hookworm disease (ankylostomiasis). This disease is very prevalent

in many tropical contries and it quite common among plantation coolies in India, but it is stated that it can be completely cured by internal administration of thymol. Another remedy which has been recommended is Chenopodium oil, the product of steam-distillation of *Chenopodium ambrosioides* or *C. ambrosioides var. anthelmintica*. Considerable controversy as to the relative merits of the two specifics has taken place during the last few years (cf Perf. and Essent. Oil Rec. 1915, *6*, 105; 1919 *10*, 139; 231; 1920, *11*, 25, 247, also Howard: The control of Hookworm Disease by the Intensive Method. Published by the Rockefeller International Health Board 1919) but the evidence appears to be distinctly in favour of thymol. Experiments tried in Trinidad, Guayaquil, America and S. India show this, and the only country where it is claimed that Chenopodium oil gave better results is Fiji. Thymol is a pure chemical compound whereas Chenopodium oil is a mixture of several substances and varies considerably with the seed and with the method of distillation. The active constituent (ascaridol. $C_{10}H_{16}O_2$.) is somewhat unstable and if the distillation is not carried out extremely carefully the oil will contain less of the active principle. E. K. Nelson (U. S. Department of Agriculture, Bureau of Chemistry, Circular No. 109 cf. J. Soc. Chem. Ind., 1913, *32*, 379.) gives full details for carrying out the distillation of Chenopodium seeds.

2. Its use for various other purposes has also been recommended. As a vermifuge it is claimed that tape-worm is expelled on the third or fourth day (Hedmann, Pharm. Central., 1903, *44*, 359, cf. Pharm. J. 1904, *18*, 206, *ibid.*, 1913, *37*, 280.) Its use has been recommended in veterinary practice for worm infested foals etc. It destroys a particular parasite known as *Strongylus tetracanthus* (ibid., 1904, *18*, 44.) It has been used as a spray in Pertussis instead of carbolic acid (*ibid.*, 1897, *4*, 361.) Its 5 per cent alcoholic solution has been used as a skin disinfectant and as a substitute for tincture of iodine (*ibid.*, 1912, *34*, 488.)

It is used as a constituent of tooth-pastes and its aqueous solution forms an ideal mouth wash. Pharm. J., 1904 *10*, 86; H. F. Goodrich, Brit. Med. J., 1917, *1*, 473.) It has also been used in odontalgia to obtund the nerve in dental caries (Pharm. J., 1898, *6*, 350.)

3. Several compounds or derivatives of thymol have also been recommended :—

Thymol-camphor, a preparation made by mixing thymol and camphor, is recommended for use in dermatological practice,

in scrotal pruritus and in pediculosis pubis and an emulsion of thymol, menthol and glycerine is sometimes used as a disinfectant (Colloid. Zeits. 1914, *14*, 253; cf. J. Soc. Chem. Ind., 1914, *33*, 665).

Glyco-thymolin is a proprietary preparation used in treatment of catarrhal conditions of the mucous membrane.

Aristol or armidol, a preparation of thymol and iodine, has been introduced as a substitute for iodoform as it is less toxic and is odourless.

Thymyl trichloroacetate, $CCl_3 \cdot CO \cdot O \cdot C_6H_3 (CH_3) (C_3H_7)$, has been used as an antiseptic for treatment of ulcers and wounds (Pharm. J. 1905, *21*, 675).

The thymyl ester of iso-valerylglycollic acid possesses therapeutic properties. It is an almost odourless, yellow liquid (J. Soc. Chem. Ind, 1913. *32*, 712; Ger. Pat. 260 471 of Nov. 25th 1911.)

The thymyl ester of *p*-carboxy-phenyl-phosphoric acid, $(CH_3) (C_3H_7) C_6H_3 \cdot O \cdot CO \cdot C_6H_4 \cdot O:PO (OH)_2$, melting at 163° is considered a valuable remedy against infectious diseases (J. Soc. Chem. Ind., 1915, *34*, 451; U. S. Pat. 1125081 of January 19th, 1915).

Thymol-phthalein, the condensation product of thymol and phthalic anhdride, (Moir, J. Chem. Met. Min. Soc. S. Africa, 1917, 17, 129; J. Soc. Chem. Ind., 1917, *36*, 571) and thymol-sulphonephthalein (Lubs and Clark, J. Washington Acad. Sci., 1915, *5* 609; 1916, *6*, 481; cf. J. Soc. Chem. Ind., 1915, *21*, 1226; 1916, *22*, 980) are recommended as indicators for special purposes, the former for estimating magnesia and lime in limestones.

The Future of Thymol Manufacture in India

1. It is obvious that if a synthetic thymol can be put on the market at six or even ten shillings per pound it will not pay, under present conditions, to grow ajowan with the idea of collecting the fruits for the manufacture of thymol.

2. At the present time the chief competitor of ajowan fruits is Spanish thyme oil. It is clear that with this oil at 11 shillings a pound for a phenol content of 45 to 50 per cent., the price of thymol cannot fall below 25 to 30 shillings a pound. The price of thyme oil is not likely to fall appreciably as wages for labour in Spain are increasing. It is probable that the cost of production from other sources such as *Monarda punctata* and *Mosla Japonica* will not be much below the cost of manufacture from

4. New methods are given for separating the thymol from the oil and for refining the former by distillation with superheated steam.

5. The yield of pure thymol form the seed was about 1 per cent.

6. Summaries are given of the sources, syntheses and uses of thymol.

7. Figures for the cost of thymol in India are appended.

DEPARTMENT OF GENERAL AND ORGANIC CHEMISTRY,
INDIAN INSTITUTE OF SCIENCE,
BANGALORE.

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