ON

EUCALYPTUS OILS,

especially in relation to their Bactericidal Power.

BY

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INTRODUCTORY.

In his Presidential Address [1] before the British Medical Association, 1903, Dr. T. D. Griffiths laid special emphasis on the value of bactericidal agents in the domain, not only of surgery, but also of medicine and therapeutics. Our knowledge of many of these remedies has within recent years been raised from "the domain of empiricism to that of science." He instanced the action of quinine in malaria, the salicylates in acute rheumatism, mercury in syphilis, as well as the actions of arsenic, iodine, iron, ozone, etc, all of which exert a greater or less antiseptic power, and the curative value of which is, in whole or in part, due to this antiseptic action.

Within the same class of remedies oil of eucalyptus may be included, as its action is mainly antiseptic. The term oil of eucalyptus is one of wide application, as it is applied to the oil obtained from any species of Eucalyptus, natural order Myrtaceae, by the process of distillation. But when we consider that there are over 120 species of Eucalyptus occurring in Eastern Australia, to say nothing of those found only in Western Australia, and that each yields an oil having a composition of its own, and differing more or less from the oils of other species, we see how general and, so to speak, vague, is the term eucalyptus oil, unless we know from what species a particular oil is derived, and what are the constituents of the oil from that species, and in what proportion they occur.

In looking over the various text-books on Materia Medica, one cannot fail to be struck by the inadequacy and inaccuracy of the statements as to the chemical composition of eucalyptus oil, in the light of recent researches on that subject.

Thus in Hale White's Materia Medica, 1898 edition, the chief constituents of the oil are stated to be (i.) a volatile oil, eucalyptol, the portion which distils between 330° and 352° F., and which is a mixture of (*a*) a terpene called phellandrene, and (*b*) cymene. It is met with in commerce. (ii.) A crystallizable resin, probably derived from the oil, and yielding ozone. (iii.) Tannin. (iv.) An oil isomeric with hydrate of cajuputene. It is met with in commerce, and is called crystallizable eucalyptol, as it solidifies at 32° F. The 1902 edition of this text-book simply repeats the foregoing, except that it states the identity of the latter eucalyptol with cineol. And yet we know now that cymene only occurs in very small quantity in the oil of one or two species, none of which are met with in commerce, and eucalyptus oil, as ordinarily used, does not contain cymene. Faust and Homeyer acted on the oil by concentrated sulphuric acid, and on adding water and distilling, they obtained a body not acted on by sulphuric acid, and which they considered presented all the characters of cymene. But this cymene was not present in the oil originally, but was formed by the subsequent action of the sulphuric acid on the terpenes of the oil. Chemists have long ago ceased to apply the term eucalyptol to the portion distilling between 330° and 352° C., but yet we find it still referred to by Hale White. Again, tannin occurs in eucalyptus leaves, but not in the distilled oil, while the resin he speaks of is found only in old oxidised oil, and is the product of oxidation of the terpenes in the oil. He says nothing of the eucalyptus pinenes.

In Potter's Materia Medica, published in 1902, he mentions eucalyptol as the chief constituent of the oil, but makes no allusion to the terpenes of the oil. Thus in both these text-books the chemistry of the oils is very badly treated of.

M. Cloëz [**2**] was the first to undertake an investigation of a eucalyptus oil, that of E. globulus. To the portion distilling between 170° and 175° C. he gave the name eucalyptol. We now know that this was a mixture mainly

of pinene, and of the true eucalyptol or cineol. He thought it did not freeze at -18°C., but in this, of course, was greatly mistaken. Faust and Homeyer [**3**] held that the eucalyptol of Cloëz was a mixture of turpentine and cymene; but, as I have just shown, their conclusions were erroneous, as cymene was not present in the oil, but was produced by the action of sulphuric acid on the terpene. They thought they were analysing the oil of E. globulus, but as they found phellandrene in the oil it must have been one of the amygdalina group.

To E. Jahns [**4**] belongs the credit of first obtaining eucalyptol fairly pure chemically, and of showing its analogy and probable identity with cineol, and that its formula was C_{10} H_{18} O.

M. R. Voiry [**5**] in 1888 discovered the method of preparing pure eucalyptol from the oil by freezing. He also detected in the oil of E. globulus the presence of acetic and formic acids, and of butyric and valeric aldehydes.

The most important work on the eucalypts, however, is that of Messrs. R. T. Baker and H. G. Smith [**6**]. In their research, extending over a number of years, the botanical characters of the eucalypts and the chemistry of their oils were thoroughly investigated. The oils of nearly every species and variety in Eastern Australia were subject to analysis, many new species discovered thereby, and many new constituents of the oil discovered and isolated. Among the latter were eudesmol, aromadendral, piperitone, aromadendrene, various esters, aldehydes, etc. These investigators classify the eucalypts into a number of groups, according as certain constituents predominate in the oils of the members of the group. Thus we have the Pinene Group, the oils consisting mainly of pinene; the Eucalyptol-Pinene Groups, the oils containing more or less eucalyptol; the "Mallee" Group, the oils of which contain eucalyptol pinene and aromadendral; the "Box" Group, containing eucalyptol pinene and a larger amount of aromadendral; the Pinene-Eucalyptol-Phellandrene

Group, the Eucalyptol-Phellandrene-Piperitone Group, and the Phellandrene-Piperitone Group. Another important result of their work was the proving of the comparative constancy of the oil of each species, no matter where grown. Formerly it was contended that the oil of a species differed according to soil, climate, etc. Much confusion had also resulted from mixing the oils of several species together. It is essential that the oil of each species be kept separate, and experimenters will then be able to get more accurate results. This is being done by many of the eucalyptus oil companies, and on the labels of the bottles they mention from which eucalyptus the oils are derived.

From a perusal of Messrs. Baker and Smith's work, it will be seen that while the botanical and chemical knowledge of the eucalypts has reached an advanced state, our knowledge of their therapeutical and physiological properties has not kept pace. We do not yet know for certain which is the chief therapeutic constituent of the oils, or whether their effects are due to the combined actions of the various constituents. When one refers to the work previously done by experimenters on the physiological and pharmacological actions of eucalyptus oil, and also to the experiences recorded by clinicians as to its therapeutic effect, one is met by many contradictions. This is in the main due to different samples of oil being used. All oils were spoken of as E. globulus oil in the early use of the drug, no matter from what species they were collected, or often they were mixtures from several species.

In the same way there was much confusion with regard to eucalyptol. The first experiments on this were done on the preparation of Cloëz (containing cineol and pinene), or on that of Faust and Homeyer (containing cineol and phellandrene), and not on the true eucalyptol or cineol. The actions of the old so-called eucalyptol and eucalyptus oil were found so much alike that the terms were often used synonymously. Thus Lauder Brunton in his Materia Medica speaks of "Eucalyptus oil, or eucalyptol as it is

often called," and Dujardin-Beaumetz refers to "l'essence oxygénée de l' E. globulus, aussi appellée eucalyptol."

Thus it is that the question has been raised as to whether eucalyptol can at all be claimed as the chief therapeutic agent in the oil, or whether the agent or agents have yet to be determined.

The main action of eucalyptus oil being then an antiseptic one, we have now to consider what medical literature has to say on the point of its antiseptic powers.

Gimbert [**7**] on injecting eucalyptol into the veins of a rabbit found that, on death immediately after, it did not putrefy, but became dry and mummified.

Siegen [**8**], using aqueous solutions 1-3800, tested the relative power of eucalyptol and quinine in preventing putrefaction when albumen was added to the solutions, and considered eucalyptol the more powerful of the two. His experiments are useless, however, as he merely went by the degree of putrefactive odour, and the relative motile activity of the micro-organisms that developed in the solutions, but which in neither case were killed. Siegen also added eucalyptol to fresh blood in the proportion of 1-300, and after ten days this gave off no foul odour. He found that mould did not form on solutions of tannin or tartaric acid when eucalyptol had been added.

Mees experimented on the same lines with eucalyptus oil, but found that greater proportions of it were necessary to prevent putrefaction than Siegen and Binz had found necessary in the case of eucalyptol. He found that the putrefaction of urine was not prevented by the addition of 1 % eucalyptol. Here then we find a variability of result, from using different preparations of varying composition. Bucholtz [**9**] worked out the question of the minimum o antiseptic necessary in a definite nutritive fluid to prevent the development of bacteria. He found that eucalypto prevented the development of bacteria in a dilution of 1 in 666.6, while carbolic acid and quinine both required to be of a strength of 1 in 200 to do the same. In the case of

carbolic acid, however, De la Croix subsequently found it to prevent the growth of aerial organisms in the proportion of 1 in 400 or 1 in 500 in meat infusion, and Koch found 1 in 850 prevented the growth of anthrax bacilli. Bucholtz's eucalyptol must have contained much ozone, yet his experiments are still quoted in the text-books to the effect that eucalyptus oil is three times as powerful an antiseptic as carbolic acid.

Schulz [**10**] treated eucalyptus oil after Trommsdorff's method by taking the crude oil, neutralising its acidity by soda solution, and exposing it in a flask, the mouth of which was closed by a plug of cotton-wool, to the action of sunlight and air, with the result that it became highly charged with oxygen in the form of ozone. He took two flasks, putting in them fresh fibrin and distilled water. To the one he added 0.01 % of eucalyptus oil, to the other 0.01 % of carbolic acid. Putrefaction was developed more quickly and was more marked in the carbolic acid flask. As he went mainly by the odor, this experiment cannot be regarded as at all exact. Schulz also preserved fibrin without decomposition for 12 months in a watery emulsion containing 1% of eucalyptus oil. He did not get so favourable a result when using the fresh crude oil. He concluded that his experiments with oxidised eucalyptus oil were in accord with those of Siegen and Mees with eucalyptol. Mees showed that ½ % eucalyptus oil was able to hinder the alcoholic fermentation of grape sugar, while quinine in a similar proportion failed to do so. Koch [**11**] found that eucalyptol 1 in 2500 impeded the development of anthrax spores, but 1 in 1000 was insufficient to arrest their development, whereas with quinine, 1 in 833 impeded the development, while 1 in 600 entirely prevented the development of the spores. Koch's results, it will be seen, differ greatly from those of the previous observers, and are far more exact. It is probable that his eucalyptol contained less ozone than that of the others. It must be remembered that the eucalyptol used by all these observers was not the pure eucalyptol or cineol, which had not at that time been isolated.

Since then not much work has been done on the bactericidal power of eucalyptus oils, while great advances have been made in their chemistry. Messrs. Baker and Smith's results have shown how useful it is for the botanist and chemist to work in conjunction, so that the latter may know the derivation of the materials he uses. So too should the physician, when experimenting, have a thorough knowledge of the chemical composition and be sure of the botanical and chemical identity of the materials he works with. In the research work, in which I have been engaged, I have been fortunate in being sure of the botanical and chemical identity of the substances used, these being in the main derived from Messrs. Baker and Smith's unrivalled collection in the Sydney Technological Museum.

The Constituents of Eucalyptus Oils.

Taking all the eucalyptus oils, 22 distinct constituents have so far been described as present in them. Many of these occur in small quantity, others occur only in one or two species, the oils of which so far seem to have no special therapeutic value. Others again are necessarily removed in the process of rectification, as they boil at low temperatures, or they are of so irritating a quality that they could not possibly be administered medicinally. Included in the foregoing categories are the following :— various alcohols such as methyl, ethyl, isobutyl, and amyl alcohols, and geraniol ; the two aldehydes, butaldehyde and valeraldehyde, which have an intensely irritating effect when inhaled, and the aldehydes citral and citronellal ; and in addition cymene, geranyl acetate, amyl eudesmate, valeric acid ester, and acetic acid ester.

There remain then for inquiry as the chief constituents of the oils, eucalyptol and eudesmol, which are oxides ; aromadendral, an aldehyde ; piperitone, a ketone ; aromadendrene, a sesquiterpene ; dextropinene laevopinene and phellandrene, which are terpenes ; and lastly acetic acid. These are all of more or less therapeutic importance.

There is one constituent found under certain conditions, which has long been held to be an important, and which I hope to prove is perhaps the most important of all, and that is ozone. The early observers found that eucalyptus oil, if exposed to light and air, absorbed oxygen from the air, portion of the oil ultimately resinifying, provided the exposure was of sufficient duration. The oxygen was in the oil in the form of ozone. This action of the oil resembled that of oil of turpentine. "Sanitas" is a watery solution of oxidised oil of turpentine, and owes its antiseptic properties to the ozone present. This formation of ozone in eucalyptus oil was explained, when the presence of certain terpenes, identical or analagous with those of turpentine, was demonstrated. Ozone is one of the most powerful bactericides we possess. Many substances owe their power in this direction to its presence or to its being set free. The chief of these is hydrogen peroxide, which possesses as strong, if not stronger, bactericidal properties than perchloride of mercury, for in a strength of 1-20,000 it prevents putrefaction in broth inoculated with sewer bacteria, while 1–125 destroys anthrax spores.

Experiments on Various Oils and their Constituents.

The following experiments on the bactericidal power of various eucalyptus oils and their constituents were performed by myself in the Pathological Laboratory of the University of Sydney by permission of Professor D. A. Welsh, and were done under his supervision.

Two test bacteria were selected for use, namely the Staphylococcus Pyogenes Aureus, as a more resistant type, and the Bacillus Coli Communis, as a less resistant one. They will henceforth be referred to as Staphylococcus and B.C.C. respectively.

Sloped agar tubes were inoculated by stroke from the stock laboratory cultures, and after 24 to 48 hours' incubation, the resultant surface growth was removed and transferred on a platinum loop to sterilized watch-glasses.

The substance to be tested was then poured into the watch-glass, and loops of the growth taken out at certain intervals of time, and transferred to the peptone-bouillon or agar tubes, which were then incubated at 37° C. for two or three days, and the presence or absence of growth noted. During the intervals of manipulation the watch-glasses were kept covered so as to prevent contamination. At first I followed Koch's method of impregnating silk threads, which had previously been sterilized, with the growth, exposing them to the antiseptic, and then washing in sterilised water, before transferring to the bouillon tubes, but as I found the method above described simpler and to answer equally well, I adopted it instead. The minute amount of antiseptic introduced on the platinum loop was found to be negligible, as it had no deterrent effect on the development of bacteria in the broth.

At the outset, as a control, and to have a standard of comparison of my results with those of other observers on another antiseptic, I tried the effect of a 2½% solution of carbolic acid in water on the bacteria I had selected for testing. Staphylococcus was killed in five minutes, loops taken from that time up to an hour all being sterile. This corresponds with the results of other observers. [**12**] With a very resistant strain of Staphylococcus, according to Abbott, some of the individual bacteria may resist the action of the carbolic acid for as long as 30 minutes, so that the strain which I was using was not a particularly resistant one. B.C.C. was killed in half an hour by the carbolic solution. This is in accordance with the fact that the typhoid-colon bacillus group is more resistant to carbolic acid than Staphylococcus, whereas it is less so with regard to other antiseptics. In all my experiments B.C.C. was the first to succumb, though in some cases it did so much more easily in comparison with Staphylococcus than in others.

Piperitone.

This substance was first isolated and its chemistry described by H. G. Smith [13]. It occurs in the group of eucalypts known as the "Peppermints," on account of the peppermint odour of the leaves. The leaves of these species have a characteristic network arrangement of the venation, this arrangement being also an indication that phellandrene is present. Piperitone was first found in E. piperita, but occurs in largest amount in E. dives and E. radiata, and in lesser amounts in E. apiculata, E. Rossii, etc. It comes over in the fraction of oil distilling between 227° C. and 240° C. Piperitone has a marked peppermint odour and taste. When placed on the tongue, it has at first a hot and pungent effect, giving place subsequently to a sense of coolness and numbness. It produces an increased flow of saliva, and when swallowed has a stimulant and carminative effect, just like other essential oils. It has a slight anaesthetic effect on the nasal mucous membrane, and causes a contraction of the vessels. Applied to the unbroken skin, it produces no appreciable anaesthesia by acting on the sensory nerves like menthol, and when dissolved in liquid paraffin and injected under the skin, I found it produced no anaesthesia. It is reputed as useful in influenza and acute coryza, and I have seen benefit from it in these conditions, and consider it well worth a further trial. It is probable that where eucalyptus oil has acted almost as a specific for influenza, it has been due to the oil being in part or in whole derived from E. dives or E. radiata, species which were at one time confused with E. amygdalina.

One drop of pure piperitone, dissolved in a few drops of liquid paraffin, and injected into the dorsal sac of a frog weighing 405 grains, after five minutes caused great restlessness, the frog jumping about vigorously. This was followed by cessation of movement. The reflexes were active for some minutes but at the end of 20 minutes they had ceased, and respiration became paralysed. The sciatic nerve when pinched caused no response in the way of

muscular movement, nor did the muscles respond when pinched. The heart was exposed and still found beating regularly and strongly. Piperitone was then applied directly to the heart and produced no effect at first, though 15 minutes later the beats became slower and irregular, and 20 minutes after that the heart stopped in diastole. Thus piperitone, in the case of the frog, acts first as a general stimulant, and then paralyses the central nervous system, respiration being quickly paralysed, while on the heart it has only a slight action. Further experiments on the physiological action of this substance should be interesting.

Piperitone is an almost colorless fluid of sp. gr. 0.9393 at $\frac{17°C.}{15°C.}$ boiling point 224-225° C., and the formula $C_{10}H_{18}O$ has been attributed to it. It is thus isomeric with eucalyptol and Borneo camphor. It probably has no optical rotation, and is soluble in alcohol ether and ordinary solvents, and slightly in water. It may be obtained in a crude condition by fractional distillation. Piperitone is a ketone, and its alcohol, which would correspond with menthol, has not yet been obtained.

As regards the bactericidal properties of piperitone, these were well-marked. The experiments to test these were conducted as above described, and verified by being repeated two or three times. The pure oil was used. Where growth occurred in the broth tubes to which loops were transferred I have signified this by the word "yes," and where there was no growth, showing that the bacteria were all killed, by the word "no."

From the table it will be evident that piperitone is strongly bactericidal to B.C.C., and less so to staphylococcus, there being a considerable difference in its action on the two, B.C.C. being killed in 40 minutes, and staphylococcus in 4 hours.

Aromadendrene.

This is a sesquiterpene occurring in most, if not all, eucalyptus oils. It occurs in greatest quantity in the oils of E. haemastoma, E. Dawsoni, E. eximia, and E.

Bactericidal Power of Pure Piperitone.

Length of Exposure.	15 Min.	30 Min	40 Min.	1 Hr.	2 Hrs.	3 Hrs.	4 Hrs.	5 Hrs.	6 Hrs.
Staphylococcus	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No
B. C. C.	Yes	Yes	No	No.	No	No	No	No	No

Bactericidal Power of Aromadendrene.

Length of Exposure.	½-Hr.	1 Hr.	2 Hrs.	3 Hrs.	4 Hrs.	5 Hrs.	5½ Hrs.	6 Hrs.	7 Hrs.
Staphylococcus	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No
B. C. C.	Yes	Yes	Yes	Yes	Yes	No	No	No	No

maculata. It is also found in the oil of Angophora lanceolata. Its chemistry was first described by H. G. Smith. [14] It is of a yellowish green color, and of an agreeable odour and not unpleasant taste, being much pleasanter to take than oil of turpentine and terebene. It is somewhat viscid and not readily soluble in alcohol. The sp. gr. is 0·9229 at 19° C., it boils at 260°-265° C. under atmospheric pressure, and is inactive to light. It has the formula C_{15} H_{24}, and may be detected by the characteristic colour reactions to bromine and acids.

It will be seen from the accompanying table that Aromadendrene kills B.C.C. in 5 hours, and Staphylococcus in 6 hours. It is interesting to note that its action on these bacilli is much more nearly equal as regards time required, than is the case with piperitone, and that piperitone is the stronger of the two as a bactericide.

Aromadendral.

Of the five aldehydes in eucalyptus oils, this is the most important as regards action on bacteria. Of the others, citral only occurs in small quantity in the oils of one or two species, citronellal makes up the greater part of the oil of one species, E. citriodora, while butaldehyde and valeraldehyde are too irritating to the bronchial mucous membrane to be of any use for administration medicinally. H. G. Smith [15] was also the discoverer of aromadendral. This aldehyde was found in greatest quantity in the oils of the "boxes" such as E. hemiphloia, E. albens, E. Woolsiana, etc., also in the "Mallees" as E. cneorifolia, E. dumosa, E. stricta, etc. Aromadendral is yellowish in tint, very mobile, with a rather disagreeable persistent odour, though some consider it not unpleasant, and its odour is masked when mixed in the oil. It is a little irritating when inhaled, but much less so than butaldehyde and valeraldehyde. It will dissolve in the usual solvents, but is only slightly soluble in water. The sp. gr. at 15° C. is 0.9477, and the rotation of light in a 100 mm. tube is $[a]_D$ —49.19° and the chemical formula C_{10} H_{14} O. It

boils at 210°-215° C. A remarkable fact is that when this aldehyde is treated with an alkaline solution of potassium permanganate, oxidation takes place with production of heat, the characteristic odour changing to one of cinnamon, and then to that of eucalyptol, one of the products formed being thus apparently eucalyptol. It is just possible that this is an indication that aromadendral is an intermediate product in the formation of eucalyptol.

Bactericidal Power of Aromadendral.

Length of Exposure.	5 Min.	10 Min.	15 Min.	30 Min.	1 Hr.
Staphylococcus ..	Yes	Yes	No	No	No
B. C. C.	Yes	No	No	No	No

We thus see that Aromadendral destroys Staphylococcus in 15 minutes, and B.C.C. in 10 minutes. As compared with the other constituents of the oils, it is a strong bactericide, being only excelled by acetic acid and ozone. It occurs only in small proportions in the oils in which it is found, except those of the "Boxes," and it certainly largely increases the bactericidal powers of these. It is also found in one oil used commercially, namely that of E. cneorifolia, but probably mostly all of it is separated off in the process of rectification, as I found the refined E. cneorifolia oil not more active than the other refined oils.

The Pinenes of Eucalyptus Oils.

Cloëz early recognized the presence of a turpentine constituent in the oil of E. globulus, and determined that it was dextro-rotatory.

Later Faust and Homeyer found a laevo-rotatory turpentine in an oil they took to be that of E. globulus, but which was most likely derived from one or more of the

amygdalina group, this laevo constituent being phellandrene.

To H. G. Smith [**16**] belongs the chief credit of elucidating the chemistry of the pinenes and determining their occurrence in the various oils. Previous to his work Bourchardat and Tardy [**17**] investigating a hydrocarbon found in E. globulus, concluded that it had the properties of the laevo-rotatory terebenthene in French oil of turpentine, but with an almost equal opposite rotation.

"It appears, then, from the results of these authors on this hydrocarbon from the oil of E. globulus, and those obtained on the same hydrocarbon from the oil from E. dextropinea, that these dextro-rotatory pinenes, obtainable from members of two distinct groups of eucalyptus, are identical, and that the dextro-rotatory pinene from the whole Genus Eucalyptus is a physical isomeride of the laevo-rotatory pinene (terebenthene) obtained from French oil of terpentine, and possibly also of the laevo-rotatory pinene of the eucalypts, although this laevo form has, so far as observed, a higher specific rotation." (Baker and Smith.)

The investigation of the pinenes of eucalyptus oil was much facilitated by the discovery of E. dextropinea, the oil of which consists mainly of dextropinene, and E. laevopinea, in the oil of which laevopinene is the main constituent, eucalyptol being almost entirely absent in both.

Dextro-rotatory Pinene.—This is a colourless mobile liquid, with an odour like that of turpentine. It has a sp. gr. of 0.875 at $\frac{4^\circ}{4}$ C.; it boils at 156° C., and has a specific rotation for sodium light of +41.2°.

Laevo-rotatory Pinene.—In appearance this resembles the dextro form, but the turpentine odour is less marked. It has a sp. gr. of 0.8755 at $\frac{4^\circ}{4}$ C.; it boils at 157° C., and rotates the ray of sodium light—48.63°. Thus it boils at a temperature 1° C. higher than the dextro form, and has a higher reverse rotation of light.

The specimens of the two pinenes that I experimented with were freshly distilled from the oils of E. dextropinea and E. laevopinea, and had not been exposed to air, thus being free from ozone. In testing the physiological action of oil of turpentine, investigators' results did not agree altogether, owing to their using oils of different chemical composition. [**18**] Koch found oil of turpentine a powerful bactericide, it destroying anthrax spores in five days, and in dilution of 1-75,000 hinders the development of anthrax bacilli. We do not know, however, the exact composition of the oil he used, what its rotation, nor how much ozone it contained. It is almost certain that his turpentine derived its activity mainly from the ozone present in it. According to Binz [**19**] when turpentine is exposed to light and air, it becomes yellowish, acid in reaction, its odour is modified, and the boiling point raised. It has the power of bleaching, and a more powerful counterirritant effect on the skin. Kingzett [**20**] considers that in ozonized oil of turpentine, the ozone exists in an organic compound C_{10} H_{14} O_4, which, when heated with water is resolved into camphoric acid and hydrogen peroxide. I shall later give reasons for believing this is not so in the case of the ozone in eucalyptus oil. It is possible that the bactericidal power of the constituents of oil of turpentine, separate and free from ozone, has not yet been worked out. My results, I hope, are a contribution towards this, if the pinenes of eucalyptus oil are really identical with those of turpentine.

I procured a sample of commercial oil of turpentine, which I found to have a rotation of $+4.5°$, and which contained a little ozone. It thus consisted of a mixture of terpenes, the dextro form being in excess. When Staphylococcus and B.C.C. were exposed to this, loops taken after an exposure of 10, 20, and 40 minutes, gave growths, but in the case of each the loop at the end of an hour was sterile. If the ozone had not been present, it would have taken longer.

I now give the results of my experiments with the pinenes of eucalyptus oils.

Bactericidal Power of Eucalyptus Pinenes.

Length of Exposure.	½ Hr.	1 Hr.	1½ Hr.	2 Hrs.	2½ Hrs	3 Hrs.	3½ Hrs	4 Hrs.	4½ Hrs	5 Hrs	5½ Hrs	6 Hrs.	7 Hrs.
B.C.C. in Dextropinene ..	Yes	Yes	Yes	Yes	No	No	No	No	..	No	..	No	..
B.C.C. in Laevopinene ..	Yes	Yes	Yes	Yes	Yes	No	No	No	..	No	..	No	..
Staphylococcus in Dextropinene	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	No
Staphylococcus in Laevopinene	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No

Bactericidal Power of Phellandrene.

Length of Exposure.	½ Hr.	1 Hr.	1½ Hrs.	2 Hrs.	2½ Hrs.	3 Hrs.	3½ Hrs.	4 Hrs.
B. C. C.	Yes	Yes	No	No	No	No	..	No
Staphylococcus	Yes	Yes	Yes	Yes	No	No	No	No

This indicates that laevopinene kills B.C.C. in 3 hours, and Staphylococcus in 5½ hours, while dextropinene kills B.C.C. in 2½, and Staphylococcus in 4 hours. Thus dextropinene was more active than laevopinene, and this is due to its greater avidity for oxygen, and consequent greater reducing power. If the two are exposed to the air, ozone appears more quickly in dextropinene.

Phellandrene.

This is the other terpene of eucalyptus oils, occurring in considerable quantity in some species, while in others it is quite absent, its place being taken by the pinenes.

Phellandrene was named by Pesci [**21**], who found it in the oil of the water fennel, Phellandrium aquaticum, where it is dextro-rotary. Wallach and Gildemeister [**22**] discovered it in eucalyptus oil, probably in that of E. dives, or one of the amygdalina group, and noted that it differed from the phellandrene previously known by being laevorotatory, which action it possesses in a high degree. Phellandrene is very unstable, and it cannot as yet be obtained quite pure. It is a colorless mobile liquid, with a turpentine odour. Its reaction with nitrous acid is characteristic.

The British Pharmacopœia test for phellandrene consists in adding twice its volume of glacial acetic acid to the eucalyptus oil to be tested in order to dissolve it, and then adding a solution of sodium nitrite, when the phellandrene will separate as an insoluble nitrite.

This test is imposed so as to exclude phellandrene from official oils as far as possible, as phellandrene is said to cause coughing when inhaled. To this I must demur. I have frequently taken 10 to 15 drops of phellandrene, and also inhaled its vapour, without experiencing any irritation of the respiratory passages to speak of, nor any tendency to cough. Moreover, I was recently administering intralaryngeal injections in a case of chronic phthisis, and on several occasions tried the effect of 10 drops of phellandrene in liquid paraffin and injected

intralaryngeally. The patient experienced no irritation and no increased tendency to cough, such as is the tendency when the aldehydes are inhaled. I cannot help thinking that phellandrene has been blamed for the misdeeds of the aldehydes. The aldehyde of E. amygdalina oil, which contains phellandrene, is of an intensely irritating character. This is a pity, as the oil is a very useful one when the aldehyde is separated, and the yield of oil from the leaves (4·215%) is higher than for any other eucalypt. It would be far more useful if the Pharmacopœia aimed at the exclusion of the aldehydes rather than of phellandrene. In addition, phellandrene is a terpene, and other terpenes are used for inhalation for phthisis, and I do not see why eucalyptus oi s containing phellandrene, which is no more irritating than other terpenes, should not be used medicinally. (See page 19).

Thus phellandrene is fatal to B.C.C. in 1½ hours, and to Staplylococcus in 2½ hours, which shows it to have stronger powers than the pinenes, and yet the Pharmacopœia seeks to exclude it.

Eudesmol.

This is the stearoptene of eucalyptus oils, and is an oxide C_{10} H_{16} O. It occurs in greatest quantity in the oils of E. virgata, E. camphora, E. macrorhyncha, etc. Eudesmol is a soft light white powder consisting of acicular and interlaced crystals. It occurs in small amount in E. globulus oil. It is insoluble in water and alkaline solutions, so I tested its bactericidal properties by dissolving it in eucalyptol and piperitone, and found it to slightly increase the activity of these, but not to any marked extent. For example, 10% eudesmol dissolved in piperitone was fatal to B.C.C. in 30 minutes, whereas piperitone itself requires 40 minutes.

Eucalyptol.

Eucalyptol has always been considered to be the most active and most important contituent of eucalyptus oils. The results which it gave in my hands tend, however, to

throw great doubt on its position in this respect, when the absolutely pure eucalyptol or cineol, free from pinene and ozone, is concerned. I have already pointed out how that the eucalyptol used by the earlier experimenters was not a simple substance, but a mixture of eucalyptol and pinene, or eucalyptol and phellandrene, and often contained much ozone. In fact, eucalyptus oil, as produced commercially after rectification now-a-days, is almost identical with the old so-called eucalyptol.

Pure eucalyptol or cineol, $C_{10}H_{18}O$, is identical with cajuputol, and occurs in other plants besides the eucalypts. It may be separated from the oil by freezing, as it solidifies at O°C., forming large colourless crystals. The pinene, which is not frozen at this temperature, may be separated off by pressure, or else by centrifugalizing. Eucalyptol is also prepared by the phosphoric acid process.

Eucalyptol is a colourless liquid, with characteristic odour, of sp. gr. 0.923, is inactive to light, and boils at 176°C. The British Pharmacopœia requires a due proportion of it to be present in eucalyptus oils by insisting that they should be of sp. gr. 0.91 to 0.93 and that they should become solid on addition of phosphoric acid, and the Pharmacopœia thus gauges the medicinal value of the oil by the amount of eucalyptol it contains.

When I started this investigation, I did so with the belief that all the constituents of the oils would be more or less antiseptic, but eucalyptol would have the greatest powers in this direction. After experimenting on piperitone, I tried eucalyptol for comparison. The specimen used was prepared from the oil of E. Smithii by freezing, and was a particularly pure specimen, as it contained but a trace of pinene and no ozone. My surprise was great when I found out how feeble were its antiseptic powers.

This first sample I have marked Eucalyptol A. The supply of this becoming exhausted, I started to check my results with a second sample, Eucalyptol B, but was perplexed at first to find it not agree with the first. This was ex-

plained when, on testing, it was found to contain ozone, and hence had greatly increased bactericidal powers. I then procured other samples (Y and S) and tested them. The specimen S was a pure eucalyptol free from ozone, and its results accorded with those of specimen A. The specimen Y contained ozone. It was then re-frozen and a few drops of pinene pressed out (see page 24); but the ozone content did not seem to be any less on again testing. Thus the ozone does not separate out on freezing. Nor does it to any marked extent on boiling, for on reference to the table it will be seen that, with specimen B, the bactericidal power is about the same after boiling for 20 minutes as before.

The results shown by the specimens A and S are indeed surprising. They indicate that when eucalyptol is pure and free from ozone, it takes eight hours to destroy B.C.C., and actually two days to kill Staphylococcus. I have purposely put down in the table a long list of loops taken, so as to show that my results are based on substantial evidence. One should also notice the very great difference displayed when ozone is present. Thus the specimen Y, which contained most ozone, destroyed B.C.C. in less than 15 minutes. It is most likely that, if ozonization has proceeded far enough, by sufficient dilutions one could get results comparable with those of carbolic acid; it is merely a matter of the ozone content, not of that of eucalyptol, which is only a very weak bactericide, and seems to play the part rather of a diluent of the pinenes and other constituents, than that of a bactericide. In this it might almost be compared to the nitrogen of the air.

I also tested the power of eucalyptol to *inhibit* the growth of staphylococcus. Agar was used for this purpose, as, being a solid at ordinary temperatures, the eucalyptol could be uniformly diffused through. A measured amount of agar was melted and sufficient eucalyptol added to make the right proportion. The tube was kept constantly shaken until the agar began to solidify, when it was

Bactericidal Powers of Eucalyptol.

Length of Exposure.	5 Min.	15 Min.	30 Min.	1 Hr.	1½ Hrs.	2 Hrs.	2½ Hrs.	3 Hrs.	3½ Hrs.	4 Hrs.	4½ Hrs.	6 Hrs.	8 Hrs.	10 Hrs.	12 Hrs.	21 Hrs	1 Day	2 Days	3 Days
Staphylococcus in Pure Eucalyptol (free from Ozone) A and S	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	..	Yes	..	Yes	Yes	Yes	Yes	Yes	Yes	No	No
B.C.C in Pure Eucalyptol (free from Ozone), A & S	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	..	Yes	..	Yes	No	No	No	No	No	..	..
B.C.C. in Eucalyptol (containing Ozone), Y ..	..	No	No	No	No	No	..	No	..	..	..	..	..	..	..	..	..	..	.
Staphylococcus in Eucalyptol (containing Ozone), B ..	..	..	..	..	..	Yes	..	No	..	No	No	No	..	No	..	..	..	..	..
Staphylococcus in Eucalyptol (B) after boiling 20 mins.	..	..	..	Yes	Yes	Yes	..	No	No	..	..	No	..	..	No	..	..	..	..
B.C.C. in Eucalyptol (containing Ozone), B ..	..	..	Yes	Yes	No	No	No	No	..	No	..	..	..	..	..	..	..	..	..
B.C.C. in Eucalyptol (B) after boiling 20 minutes ..	..	..	..	..	Yes	No	No	No	No	No	.	..	..	..	No	..	..	.	..

sloped. The tubes were then inoculated with Staphylococcus by stroke, and incubated at 37°C. With eucalyptol in the proportions of 1-10, 1-20, 1-30, there was no growth, 1-35 gave a few feeble colonies, 1-40, and 1-50, gave a larger number of colonies, 1-60, 1-80, 1-100 gave a growth which was delayed but ultimately abundant. Thus it takes a strength of 1-30 of pure eucalyptol in agar to absolutely prevent the growth of Staphylococcus.

Crude Eucalyptus Oils.

Having thus investigated the bactericidal properties of the chief constituents of the oils, one was able to form a pretty fair estimate of what would be the results when the oils themselves were treated. When I started on the crude oils, however, the results were at first perplexing and corresponded not at all to what one got with the constituents and the refined oils. I found that the differences were to be explained by the presence of the free acid in the oils. This acid in all cases is acetic acid. The deep red or brown color of some crude oils is due to their dissolving some of the iron of the stills. If copper stills are used, a greenish tint may be given. Both acetic acid, iron, and copper are bactericidal, but of course the acetic acid is of most consequence in this connection. An acid medium in itself is unfavorable to bacteria.

I tested the reactions of the crude oils in my possession, and found them as follows :—Those of E. globulus, E. cneorifolia, E. Smithii, E. cinerea, E. camphora, E. apiculata, E. Macarthuri, E. punotata, E. eugenioides, E. odorata, and E. amygdalina were all markedly acid, while those of E. citriodora, E. dives, E. Dawsoni, E. hemiphloia, E. macrorhyncha, E. piperita, and E. dumosa were either neutral or very faintly acid. A reference to the tables given of the bactericidal powers for the two bacilli, shows that the acid oils are the most active, this being due entirely to the acid. When the acidity is neutralized by soda solution without any other rectification, a great difference is manifested. Thus crude

E. Smithii oil destroys Staphylococcus in 30 minutes, but after neutralizing it takes 3½ hours to destroy it. As, for medicinal use, the oils are always rendered neutral, knowledge of the bactericidal powers of the crude oils is not a very great help.

Bactericidal Action of Crude Oils on B. C. C.

Length of Exposure.	15 Min.	30 Min.	1 Hr.	2 Hrs.
E. globulus	No	No	No	No
E. eugenioides	No	No	No	No
E. cneorifolia..	No	No	No	No
E. amygdalina	Yes	No	No	No
E. punctata	No	No	No	No
E. Smithii	No	No	No	No
E. citriodora	Yes	No	No	No
E. cinerea	Yes	No	No	No
E. camphora	Yes	Yes	No	No
E. dives	Yes	Yes	No	No
E. hemiphloia	Yes	Yes	No	No
E. piperita	No	No	No	No
E. macrorhyncha	Yes	No	No	No
E. apiculata	No	No	No	No

The bactericidal power of the neutral or only slightly acid crude oils is due mainly to the presence of their other constituents such as aromadendral in E. hemiphloia, piperitone and phellandrene in E. dives, E. amygdalina, etc. Apart from the presence of acid and of ozone, the aromadendral oils as E. hemiphloia may be considered the

most powerful bactericides, but it is not certain whether they could be used medicinally.

Bactericidal Action of Crude Oils on Staphylococcus.

Length of Exposure.	20 Min	30 Min	40 Min	1 Hr.	2 Hrs.	3 Hrs.
E. Smithii	Yes	No	No	No	No	No
E. globulus	Yes	Yes	No	No	No	No
E. cneorifolia	Yes	No	No	No	No	No
E. cinerea	Yes	Yes	No	No	No	No
E. punctata .. .	..	Yes	..	No	No	No
E. dives	..	Yes	Yes	Yes	No	No
E. hemiphloia	..	Yes	Yes	No	No	No
E. amygdalina	Yes	Yes	..	Yes	No	No

Refined Eucalyptus Oils.

The bactericidal power of the refined commercial oils does not at all correspond to that of the crude oils. It may be stated to be the mean of those of the constituents of the oils. Thus, if equal parts of eucalyptol and pinene were mixed, the bactericidal power would be intermediate between those of eucalyptol and pinene separately. The mixing does not seem to give any increase in power.

When the oil has been exposed to air, and ozone is present, the bactericidal power is very greatly increased. Thus the oil of E. Smithii destroys Staphylococcus in 6½ hours, but when a small amount of ozone was present it did so in less than 2 hours. Similarly globulus oil takes 7 hours to kill Staphylococcus, but when ozonized it will be seen that it kills B.C.C. in ½ an hour.

To know of this wide variability in the commercial oils, which yet may be up to the Pharmacopœial standard, is of very great importance. It is a surprising fact that these oils when free from ozone take from 6 to 9 hours to

Bactericidal Power of Refined Eucalyptus Oils.

Length of Exposure	15 Min	30 Min	1 Hr.	2 Hrs.	3 Hrs	4 Hrs.	5 Hrs	6 Hrs.	6½ Hrs	7 Hrs	9 Hrs.	12 Hrs
Staphylococcus in E. globulus .. .	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No
Staphylococcus in E. cneorifolia ..	Yes	..	Yes	Yes	Yes	..	Yes	Yes	..	Yes	No	No
Staphylococcus in E. amygdalina ..	..	..	..	Yes	No	No	No	..	..	No	..	..
Staphylococcus in E. Smithii	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	..	No	No
Staph. in E. Smithii (conta'ng Ozone)	Yes	Yes	Yes	No	..	..	..	..	..	..	..	..
B.C.C. in E. globulus (conta'ng Ozone	Yes	No	No	No	No	..	..	..	..	..	..	..
Staphylococcus in E Cinerea	Yes	Yes	Yes	Yes	Yes	Yes	Yes	..	..	No	No	No

destroy Staphylococcus, while when ozone is present they take 2 hours or less. I had three samples of oil sent me, the circular accompanying them setting forth that the E. Smithii oil was of the highest grade, E. cinerea oil a good grade oil, and the E. amygdalina an inferior grade oil. Yet what do we see? The E. Smithii oil (which had no ozone) took 6½ hours to kill Staphylococcus, the E. cinerea one took 7 hours, while the E. amygdalina oil (which contained ozone) took only 2 hours.

It seems a great pity that the British Pharmacopœia makes no demands as to the presence of ozone.

By prolonged exposure of a crude oil to sunlight and air, I have succeeded in getting a fairly large amount of ozone in it, but unfortunately have not had time to experiment on it before the writing of this thesis.

Ozone.

Much has already been said as to the presence of ozone in the oils of Eucalyptus. It will be evident from the experiments already detailed, that this is the chief bactericidal agent in the oils, and that the oils free from it —as seems to be the case more often than not — are comparatively weak in their action on bacteria. Especially is this weakness evident where eucalyptol is concerned. But to which of the components of the oils is the presence of ozone due? It is to the terpenes.

When the pinenes, phellandrene, and aromadendrene are exposed to the air on a piece of paper, they do not turn starch and potassium iodide blue at first, but this re-action begins to appear after about 20 to 30 minutes, and the pinene or other terpene then resinifies. Phellandrene and aromadendrene "ozonize" more quickly than dextropinene, and the latter more quickly than laevopinene.

Aromadendral, eucalyptol and piperitone only develop ozone in the very slightest degree, and this is due to it being almost impossible to free them entirely from small traces of the terpenes. Eudesmol is rather unstable and it is just

possible that its oxygen may, under certain circumstances, be given off, and the eudesmol be reduced to terpene.

I have said that several of the specimens of eucalyptol I experimented on contained ozone. How then did they come by that ozone ?

I have shown that boiling does not make much difference in the ozone content of eucalyptol, nor does freezing do so either.

The ozone must, therefore, have been formed by the terpenes of the original oil and to have been uniformly diffused through all the constituents of the oil. When the eucalyptol was separated out by freezing, the ozone held by it would be contained in the crystals of frozen eucalyptol, while the rest of the ozone would be separated off, by pressure, in the pinenes and other constituents. We know that ozone is not decomposed into oxygen until a temperature of 250°—300° C. is reached. Hence, when the earlier observers prepared their so-called eucalyptol from the ozonized oil (which they seem generally to have done, and a very highly ozonized oil too), by distilling off the portion boiling at 170°—175° C., then most of the ozone would have come over with the eucalyptol without decomposition, and hence their results with eucalyptol would be almost identical with those for the original oil.

The eucalyptol readily gives off its ozone, as may be shown by the following experiment :—Equal parts of eucalyptol (containing ozone) and water were shaken for several minutes in a test-tube. They were then allowed to separate out again into two layers, accordiag to specific gravity, the eucalyptol, of course, rising on top. On then testing for ozone with potassium iodide and starch, the water was found to contain part of the ozone, and gave equally as blue a colouration as the eucalyptol.

From this we can understand how the earlier observers when they introduced a small amount of eucalyptus oil or eucalyptol, charged with ozone, into a nutrive fluid, found putrefaction prevented, this being due to the ozone from the

droplet introduced diffusing through the nutritive medium, while the oil itself would rise to the surface and exert little or no retarding influence. In my experiments I invariably found that the small droplet of oil or eucalyptol, introduced along with the dead or living bacilli, had no effect in preventing the growth of the bacilli if they were alive.

If eucalyptus oil be valued medicinally chiefly for its power as an antiseptic, then we must regard ozone as its most valuable constituent, and next to this the pinenes and other terpenes, as they are not only antiseptic in themselves, but are the agents in the production of the ozone. Piperitone also seems likely to prove a valuable constituent, and is well worth further trial. Eucalyptol we must regard as the weakest antiseptic of all, and to be chiefly valuable as a carrier of ozone. It also helps to dilute and cover the taste of the rather nauseous terpenes, and make the oil more palatable and more pleasant for inhalation.

It seems to be the custom of most eucalyptus oil companies to bottle their oil immediately it is prepared and rectified, and keep it shut off from the air. This I would strongly deprecate. I would recommend that the oil be stored for at least two months in vessels, the mouths of which are closed by a plug of cotton-wool, and that they be shaken every day or two so as to expose a fresh layer of oil to the influence of the atmosphere. The action of the sunlight seems to be important also in the formation of the ozone. In this process very little of the oil is lost by evaporation.

The Australian Eucalyptus Oil Company, I find, do expose their oils to the action of the atmosphere. Another matter that presents itself is that the amount of ozone developed must depend on the amount of terpene present, and it is therefore necessary to ensure that a proper proportion of this is present in an oil.

Again, the preparation of eucalyptol from an ozoneless oil is not to be recommended, but if it is prepared from an ozone-containing oil, it, as I have shown, takes up the greater part of the ozone—because eucalyptol

generally occurs in largest proportions in the oil—and hence an ozone-containing preparation may be regarded as very valuable medicinally. It must be remembered that the proportion of ozone in both oil and eucalyptol is sure to vary within wide limits.

Pharmacology of Eucalyptus Oils.

A typical eucalyptus oil, for instance one of the eucalyptol-pinene group, may be considered to resemble oil of turpentine very greatly in its action on the body.

This action being in the first place chiefly an antiseptic one, we may inquire how this antiseptic action is brought about. Binz contended that in the case of oil of turpentine, this is performed in two ways. Firstly, the oil has a great affinity for oxygen, and will abstract it from wherever it can ; from the air if possible, and when in the body or in contact with the body, from the protoplasm of tissue and other cells, such as those of bacteria. In this case, it acts as a reducing agent. Secondly, having got the oxygen, often in the form of ozone, it is ready to part with it again to the protoplasm of tissue and bacterial cells, and hence this action is an oxidising one, and is generally the more energetic of the two, especially if ozone is present in any quantity. This deprival or addition of oxygen probably causes such a change in the chemical composition of the protoplasm, as to cause death of the cell. Schulz claimed that the terebenthene of eucalyptus oil acted in the same way, and now that more is known of the occurrence and constitution of the pinenes of the oils, and also of phellandrene and aromadendrene, it is probable that these all act in the same way.

The other constituents of the oils probably act as direct poisons to the bacteria, or else they may enter into some chemical combination with the protoplasm of the cell, and so render the continued life of the cell impossible.

The external counterirritant action of eucalyptus is the same as that of turpentine, only less energetic. The actions of eucalyptus oil when taken internally are also

almost identical with those of oil of turpentine, and need not be re-capitulated here. On the nervous system it is a more marked depressant than turpentine. It may be that the experiments demonstrating this were conducted with a piperitone-containing oil, and piperitone, as I have shown, causes marked depression of the nervous system when injected into frogs.

Eucalyptus causes contraction of the spleen. To what constituent this is due is at present undetermined.

The action of eucalyptus in malaria is also interesting. Tristani and also Brunel [**23**], using an infusion of the leaves, were the first to report success in the treatment of this disease. Castan cured 15 cases out of 27, by using the powdered leaves and also the infusion. Keller [**24**], employing Lorinser's tincture of eucalyptus treated 432 cases, and obtained a cure in 310, or 71%. Of the 432 about 28% had already been treated by quinine without effect. Lorinser himself, with his tincture, obtained success in 43 out of 53 cases. Schulz also found the ~~ozonized oil~~ tincture successful. Others, on the other hand, reported failures, as Papillon, who used the powdered leaves, but in such a way that they provoked diarrhœa, and an alcoholic extract, and Burdel, who only obtained a small proportion of cures. To what constituent of eucalyptus we may attribute an action in malaria is so far quite undetermined. Oil of turpentine is not considered to have any antiperiodic action, so we can hardly put it down to the terpenes of eucalyptus. Nor is cineol, as obtained from other plants, credited with any activity. It may, therefore, be possibly due to a combination of factors. When the leaves or an infusion or tincture of the leaves are used, other constituents of the leaves besides the essential oil may contribute to the result. When the ozonized oil is used, the result may possibly be due to the ozone, the ozone being perhaps introduced in the body in the oil in such a way that it is active against the plasmodium malariae, where ozone in other forms would be inactive. The action of certain antiseptics in certain diseases seems to be a specific one,

and not dependent on the relative strength of the antiseptic. Thus quinine is effective in malaria, whereas perchloride of mercury, a far more powerful antiseptic, has no influence. Similar is the effect of the salicylates in acute rheumatism. Quinine seems to cause its effect, not by directly destroying the malaria parasites in the blood, but by producing an environment unsuitable to their existence, and also by preventing the appearance of the young forms in the corpuscles.

Eucalyptus in large doses lowers the temperature. It is absorbed from the skin, alimentary canal and respiratory mucous membrane, and is excreted by the skin, the kidneys and the expired air. In the urine the terpenes are excreted partly unchanged, partly as compounds of glycuronic acid, and impart an odour of violets, just as in the case of turpentine. The eucalyptol is probably excreted unchanged. Eucalyptol has probably very little toxic effect, as, as much as 10 grammes of the oxidised oil (which would contain only a very small proportion of terpenes and consequently would consist mainly of eucalyptol), have been taken daily without any effect to speak of.

Therapeutics.

External.—On account of its antiseptic power Lister strongly recommended eucalyptus oil as a surgical dressing in the form of gauze lotion or ointment. These were formerly much used, on account of the greater toxicity of carbolic acid than of eucalyptus. If ozone is the chief antiseptic of the oils, I do not see how it could be expected that eucalyptus gauze could contain any. An ozonized oil, however, would be useful in the form of lotion or ointment, especially as the ozone is given off by the oil to the water it is mixed with. Eucalyptus oil has been used locally with benefit in a variety of conditions, such as ozaena, laryngeal diseases, diphtheria, gonorrhœa and leucorrhœa, as a rubefacient in rheumtism, as an inhalation in phthisis, gangrene of the lung, bronchitis, and ozaena. It has been

recommended to substitute eucalyptol for the oil for use on the oro-nasal inhaler, because the former does not form a varnish on drying. This I would strongly advise against, unless it be known that the eucalyptol contains a fair amount of ozone. The very fact of a varnish forming, when the oil is used, indicates the formation of ozone.

Similarly we can understand the efficacy of the continuous inhalation of eucalyptus vapour in the treatment of diphtheria, scarlet fever, whooping cough, and influenza. The air of a room with eucalyptus vapour in it contains a good deal of ozone.

Eucalyptus oil has for long been a popular remedy for influenza and acute coryza, and it appears to do good in these cases. I should consider the piperitone oils best for this purpose.

Eucalyptus oil has been used as a remedy in cancer, and its usefulness in this disease has lately been re-affirmed.

INTERNAL.—Eucalyptus oil may also be used internally for bronchitis, phthisis, and other chest diseases, as well as by vapour and inhalation. Taken internally it is excreted by the bronchial mucous membrane. Its action would be a double one, reduction and oxidation. The oxygen of the inspired air coming in contact with this excreted oil would materially aid in the process.

For pyaemia, puerperal fever, and septicaemia, eucalyptus oil has been used as a hypodermic injection in olive oil. In some cases very great benefit has resulted, and the good results followed so immediately that the oil seemed to act almost as a specific. In other cases, little or no good has followed the use of the oil. This I believe to be because different varieties of the oil have been used, some of them containing no ozone.

The following case will be of interest :—

A girl aged 15 years, was attacked with erysipelas of the middle third of the leg. She was put on a mixture of quinine and iron, 1½grs. of quinine being given

every 6 hours, and the leg was dressed with an ointment of carbolic acid and ichthyol. In spite of this she continued to get worse, the temperature keeping between 102° and 103° F., and the erysipelas had extended as far as the ankle and knee. Then on the 5th evening, when the temperature was at 103° F., m. vi of ozonized Eucalyptus Smithii oil in glycerine were given hypodermically just above the knee. In half an hour the temperature fell to 101° F., and next morning had fallen to normal, and patient felt much better. That night the temperature rose to 100°, and the following evening patient was worse again, the temperature being 102° F., and the erysipelas had spread over the foot and also extended $1\frac{1}{2}''$ above the knee. The quinine and iron mixture was then stopped, and the hypodermic of m. vi of the oil repeated, when the temperature fell to normal again in a few hours. The injections were given night and morning for the next few days, and patient's temperature kept down at normal, the erysipelas disappeared, and she convalesced rapidly. The benefit from the use of the oil in this case was undoubted, and it acted like a charm. Success has also attended the use of eucalyptus oil in scarlet fever, and where want of success has been reported, I would suggest that it has been due to an oil, free from ozone, being used. Eucalyptus oil has also been used in typhoid fever. Its great advantages are that in medicinal doses it acts as a mild stimulant, it is an antiseptic, and it also slightly reduces temperature. I have at present several cases of typhoid under treatment with this remedy. It seems to act very efficiently, but it is as yet too early to speak definitely of them, as they are still undergoing treatment. I hope later to report the results. Eucalyptus oil and various preparations of the leaves, as already stated, have been extensively used in malaria, with good results in many cases. It seems most efficient in cases of quartan ague that resist the action of quinine. I would suggest that a thorough trial be given of the use of the ozonized oil by hypodermic injection in malaria.

Mention must also be made of the use of an infusion of E. globulus leaves in diabetes. Faulds [**25**] reports having tried it in 46 cases, of which 15 were quite cured, and with the others there was a marked diminution or even complete cessation of the glycosuria during its use. He found the oil or eucalyptol to have no effect in these cases.

I have recently treated a case of diabetes on similar lines. I first used an infusion of the leaves of E. punctata. The amount of sugar was reduced from about 60 grains daily to about 12, but it would go no lower. I then used the infusion of the leaves of E. globulus. The effect was apparent at once. The sugar disappeared entirely, but reappeared when the use of the infusion was discontinued. Evidently the substance which prevents the glycosuria exists in the leaves of E. punctata in small quantity but in the leaves of E. globulus in considerable quantity. What it is, we do not at present know, though I am at present investigating this interesting question.

In presenting this thesis, I do so with much diffidence, in as much as many of my conclusions are at variance with views previously held. This applies more especially to views held as to eucalyptol being the most important constituent of the oils. My conclusions, however, are based on a large number of exact experiments, which were verified in most cases by being repeated two or three times.

The importance of the presence of ozone in the oils has for long been recognised, and my results strongly support and emphasise this view. Piperitone, too, if given a trial may prove of marked therapeutical importance.

In conclusion I desire to express my grateful thanks to Professor D. A. Welsh, of Sydney University, for enabling me to carry out these experiments, to Messrs. R. T. Baker and H. G. Smith for their specimens of oils, and also to the Australian Eucalyptus Oil Co. and Messrs. Faulding and Co. for their samples of oils.

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