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STUDIES IN THE GENUS MENTHA.*†

XII. *Mentha piperita*, L. (Peppermint) as a Subject for Biochemical Research.

BY F. J. BACON, G. C. JENISON, AND R. E. KREMERS.‡

Students familiar with the range and variety of phenomena coming under the observation of pharmacists have often remarked upon the ignorance or indifference of other scientists to the possibilities for research upon these phenomena. To sketch the development of problems connected with a pharmacopœial substance into researches of very general interest is the object of this paper. The U. S. P. oil of peppermint, which was the original object of study, is not a natural oil, but one rectified to conform to certain standards. Since the peppermint industry is one of the largest in this country producing an essential oil, the problems connected with the growing plant as well as with the distillation of the oil are of obvious importance.

In order to become more familiar with this industry, the Wisconsin Pharmaceutical Experiment Station has been growing peppermint on a semi-commercial scale. The chemical studies at first concerned the recovery and identification of the compounds remaining in the aqueous distillate.^{1,2} In 1921 acetone and methyl-I cyclohexanone-3 were found in these materials.³ These substances result from the hydrolysis of pulegone, which in its turn was sought and found.⁴ It was also observed that another mint, imported as a Japanese peppermint and growing in an adjacent field, was producing pulegone instead of menthol. These results at once suggested the existence of a common fundamental metabolism for oil production and offered a possibility for experimental investigation of the idea.

The further study of this proposition soon revealed that botanists consider

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¹ E. R. Miller, *Bull. U. W., Circ.* 9, Feb. 1920.

² R. E. Kremers, *Ibid.*, *Circ.* II, Oct. 1920.

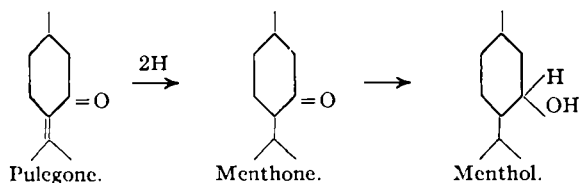
³ R. E. Kremers, *Jour. A. Ph. A.*, 10, 834, 1921.

⁴ R. E. Kremers, *Jour. Biol. Chem.*, 52, 443, 1922.

M. piperita a hybrid,¹ whereas the menthol yielding plant of the Japanese is referred to *M. arvensis*, a true species. Thus the original simplicity of comparison was destroyed, but a vastly bigger problem could be visualized. If our common peppermint is a hybrid, and if the production of oil results from a definable process,² then the changes brought about in the oils by hybridization should lead to a clearer conception of hereditary processes. This is the problem toward which we have been working during the past year, more particularly to verify the premises.

The scope of the problem is enormous. In the first place, it has been necessary to establish with exactitude the definition of the "species" *M. piperita*. This was a research in itself, requiring the assembling and comparing of all original descriptions. Where original publications were not available, photostatic reprints were obtained. It is also necessary to attempt the experimental production of a "peppermint" by hybridization as a check upon the morphological deductions of the botanists.

On the chemical side, a prerequisite is a complete knowledge of the composition of the oil³ so that both qualitative and quantitative variations may be followed from year to year. It has been found that methyl-cyclohexanone is not always present, and it is possible that the reported occurrence was due to the treatment to which the oil was subjected. But its precursor pulegone, and possibly piperitone, appear to be constantly present. This seems to be highly significant; for in the genus *Mentha*, pulegone and menthol are the only substances known to attain to 80 per cent. of the oil. This suggests that a menthenone is formed first, and that the menthone and menthol considered characteristic of peppermint are formed from it by reduction:



Since piperitone gives isomenthones,⁴ whereas pulegone appears to give ordinary menthone,⁵ when reduced by palladium and hydrogen, it may be possible to trace these relationships very definitely.

This hypothesis must be accepted cautiously. Should it truly explain the origin of menthol, only a part of the whole fundamental biochemical process would have been elucidated. However, it is encouraging to find evidence which supports the premise of a biochemical process of oil production.

While these results are significant for biochemical theory, they are equally so for pharmaceutical practice. It is only a question of how the application is made. The finding of the menthenones in peppermint oil has influenced our biochemical theories and at the same time suggests a means of improving the quality

¹ On the authority of Briquet, cp. Tschirch.

² Ref. to R. E. K., *Jour. Biol. Chem.*, 50, 31, 1922.

³ N. b. the classical work of Power and Kleber.

⁴ Hughesdon, Smith, and Read, *C. A.*, 17, 1222, 1923.

⁵ Jenison and Kremers, unpublished research.

of the oil. Should the latter be sufficiently great, it will undoubtedly be reflected in commerce and in the Pharmacopœia.

Another instance of the kind may be selected from our work. The aldehydes¹ present to a very slight extent in the natural oil are highly important in the suggested scheme of biochemical oil formation. On the other hand they are now refined away during rectification because of their objectionable properties. To study them more closely, material representing 12,000 pounds of natural oil² was worked up, yielding approximately 500 Gm. of isovaleric aldehyde. The mere handling of such a quantity of material suggests to the thoughtful experimenter ways of utilizing a by-product.

Although only a few of the more important developments have been sketched, we hope to have shown that a prosaically common pharmaceutical article like oil of peppermint may offer a little universe of fascinating ideas and problems to the inquisitive mind. We hope that the dispenser of this oil will share with us the sense of pleasure which these ideas bring and will regard his bottle of oil as a connecting link between himself and the living out of doors.

PROGRESS IN VITAMINE RESEARCH.*

BY CASIMIR FUNK AND HARRY E. DUBIN.

Vitamine research has advanced along three lines: first, the demonstration of the actual existence and the nature of specific vitamins; second, the study of the vitamine content of various foodstuffs, raw and cooked; third, investigation of the chemistry of the vitamins.

As regards the chemistry of the vitamins, little of real significance has been accomplished. A number of vitamine concentrates have been made by various investigators, while we ourselves have prepared concentrates from yeast and cod-liver oil which are approximately from five thousand to ten thousand times as active as the starting material. Nevertheless, despite this high degree of concentration, we are still far removed from the isolation of the various known vitamins and the determination of their chemical composition.

The study of the vitamine content of different foodstuffs is of practical importance in that particular dietaries may be chosen with confidence in the effects they will produce. In this direction, our knowledge of nutrition has been materially augmented.

However, it is the demonstration of the existence of specific vitamins which has spelled the greatest progress. Until very recently, only three vitamins were known:

A—The antirachitic vitamine, found in certain fats and oils and in the leafy parts of some vegetables.

B—The antiberiberi vitamine, occurring in a variety of grains, vegetables, fruits and in yeast.

C—The antiscorbutic vitamine, present in certain fruits and vegetables.

¹ Ref. to R. E. K., *Jour. Biol. Chem.*, 50, 31, 1923.

² Generously furnished by the A. M. Todd Co., of Kalamazoo, Mich.

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