Recent Development in the Vitamins of Oils and Fats*

By Kenneth K. Jones

OF the seven, or possibly eight, vitamins found in food, we are concerned with three only in the oils and fats—the vitamins A, D and E. Funk coined the word *vitamin* to designate the active principle in his yeast extracts which cured polyneuritic pigeons in such a striking and spectacular manner. "The life-giving amine," he called it, because his analyses of this material showed nitrogenous ingredients. Now, although his first ideas have been shown to be wrong in many points, the word *vitamin* is accepted by the world. Few other concepts have captured the popular imagination as has this vitamin concept.

Now billboards ask us whether we have had our sunshine vitamin, newspaper columnists write of vitamins, and even of late the crooners over the radio insist that they are "full of vitamin A."

Few, however, stop to think that the word *vitamin* is synonymous with the expression x in an algebraic formula; that it stands for an unknown quantity in nutrition, and that as soon as this substance is isolated and analyzed it will no longer be a vitamin, and that many substances used in nutrition would be vitamins, if the chemical nature were unknown. Iodine, iron, linolenic acid, and tryptophane would be such vitamins. One interesting fact distinguishes the vitamins from other nutrients. This is the fact that the vitamins are needed only in exceedingly small amounts.

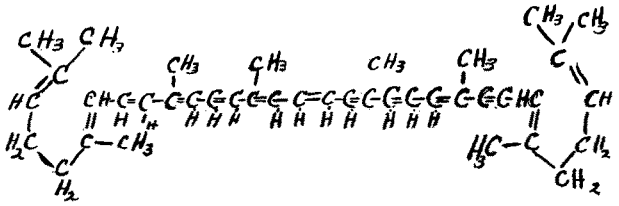
We now know that the lipoidal substances have an important and specific role to play over and above that of furnishing a convenient and concentrated source of energy, that from the fats and oils we get the vitamins A, D and E, the unsaturated fatty acids, linolic or linolenic, as shown by Burr and Burr, and compounds similar to lecithin or cephalin.

The story of the discovery and development of these vitamins you already know. One of the early observations indicated that vitamin A activity was associated with the prevalence of a yellow pigment in foodstuffs. The interesting development of recent years is the proof that this yellow pigment is the source of vitamin A, though for over ten years after Steenbock and Boutwell first made this claim, this interesting correlation was ignored, principally because Palmer showed clearly that vitamin A activity need not be associated with pigment.

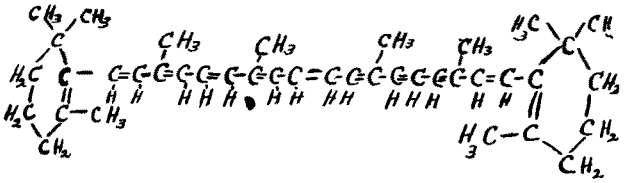
Recently Moore and von Euler have shown that the yellow pigment *carotene* is the forerunner of vitamin A and that pure crystalline carotene can be converted into vitamin A in the animal body. Moore and Capper have found that .001 mgm. of pure carotene is able to bring about cures in rats on diets deficient in vitamin A.

According to Karrer, the pigments of tomatoes, lycopin, and the pigment of carrots, *carotene*, have the same empirical formula $C_{40}H_{56}$ but that lycopin will take up 13 oxygen atoms or 26 hydrogen atoms to form the compound $C_{40}H_{82}$, a saturated hydrocarbon, while carotene becomes saturated with 11 oxygen or 22 hydrogen atoms to form the saturated compound $C_{40}H_{78}$.

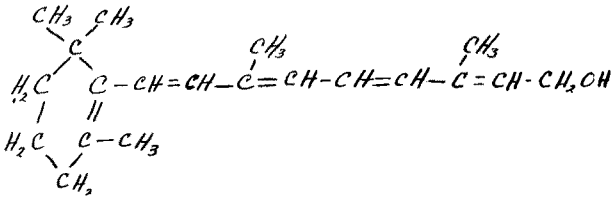
This is due to the condensation of the end groups of the lycopin chain to form two benzine rings. Lycopin is a straight chain with isoprene linkages. Written as follows, the condensation which may be effected becomes more evident than if the formula were written in the regular way:



By the condensation of the end groups into benzene rings, the compound carotene is formed.



According to Karrer, this molecule breaks into two molecules of vitamin A, which has a molecular weight of approximately 300 and on oxidation breaks down into the same compounds as the parent substance does.



Karrer substantiates this with spectroscopic studies showing that vitamin A has five double bonds in agreement with the formula as given above.

This clears up one problem of the relationship between pigment and vitamin A, but leaves us with the question whether carotene as well as vitamin A is needed by the animal body.

The relation of vitamin A to the physiology of the animal has come in for much investigation recently. Outstanding in this is the evidence which points to vitamin A as a factor in promoting the healthy condition of the mucous cells and tissues of the body. Cramer has shown that there is atrophy of the mucous-secreting cells and necrosis of the villi of the intestine in the absence of A vitamin. He also has found in this condition that B. Coli is able to pass from the intestines, through the intestinal wall into the blood stream. From this it is evident that the chief role of this vitamin is to keep up the first line of defense in the mucous surfaces of the body. The vitamin is therefore more concerned in preventing infection than in curing it. This is particularly true of the recent idea that vitamin A is a cure for the common cold.

In connection with this injury to the mucosa, Aberle has shown that the first definite symptom of the lack of A vitamin is the appearance of cornified epithelial cells in the vaginal smear from rats and that this is true in one hundred per cent of the cases observed. This makes, therefore, a very sensitive and accurate test of vitamin A.

When Mellanby found that various oils and fats would cure the rickets that had developed in puppies he was

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raising on foods deficient in fat, he believed that the curative factor was the vitamin A in the fats he fed back. Others repeated these experiments with more or less success, but it was soon noticed that many fats which were very effective in curing zerophthalmia in rats would not effect the cure of rickets, and on the other hand some fats would improve the rachitic condition without having any effect on zerophthalmia. McCollum and his collaborators settled this question by bringing forth convincing evidence of a new vitamin. This evidence was obtained by destroying the vitamin A in cod liver oil by oxidation and by intact showing that the anti-rachitic principle still remained in the oxidized oil.

Rollier and Huldinsky at this time were demonstrating that ultra violet light either from the sun or from an artificial source would cure rickets. This seemed to complicate the situation, until it was observed that rachitic rats kept on sawdust that had been accidentally irradiated with ultra violet light were cured. This fact led Hess and Steenbock to carry out a series of experiments from which both at nearly the same time announced the fact that irradiation with ultra violet light would confer antirachitic properties on certain foodstuffs, and especially on those which contained non-saponifiable matter or cholesterol.

From this it was but a step to show finally that the provitamin was ergosterol, a sterol first discovered by Tanret in 1888, and which is found along with cholesterol in nearly all tissues. The irradiation of one-tenth per cent solution in ether for thirty minutes produces the maximum activity of vitamin O. This irradiated ergosterol is then dissolved in neutral oil and is called viosterol.

At present ergosterol is obtained commercially from the lipoids extracted from yeast. The yeast plant contains from .2 to 1 per cent of this sterol.

Vitamin D is not only formed from ergosterol by irradiation but also is destroyed if the irradiation is prolonged, so that a definite amount of radiant energy must be given at the most effective wave length, which lies between 280 and 302 milli microns.

Ergosterol is supplied to the body in the food, and also, as shown by the work of Koch, it may be synthesized in the body from cholesterol. It is evident from recent work that ergosterol is present in the skin, especially in the sebaceous glands. Ultraviolet light penetrates the skin only for a few millimeters, but this is sufficient to form vitamin D.

The English workers, Angus, Askew et al., and the German workers with Windaus have both obtained similar crystalline products from irradiated ergosterol, but these as yet are not pure nor do they contain all the activity of the irradiated ergosterol. The indications are, however that vitamin D will soon be established as a definite chemical compound and its formula determined. Vitamin D is not precipitated by digitonin, is not readily destroyed by heat or oxidation, and is so potent that .00002 of a milligram will instigate healing in a rachitic rat.

This development of active irradiated ergosterol solutions of great potency has given rise to some physiological findings of clinical importance in the metabolism of calcium and phosphorus, for it has been shown that both calcium and phosphorus must be considered together in discussing rickets. If the calcium and phosphorus in the food are in the same ratio as found in bone, that is, between 2:1 and 1:1, it is exceedingly difficult to give an animal rickets even if there is no vitamin D in the diet. If the ratio varies far from this either way, it requires more and more vitamin D to keep the animal from getting rickets. Part of this has been shown to be due to increased difficulty of absorption and that one important function if not the most important function of vitamin D is to aid in or make possible the absorption of calcium through the intestinal wall.

At first it was claimed by Taylor that the action of vitamin D in raising the level of blood calcium was a stimulation of the parathyroid glands, since it is well known that the secretion from this gland is potent in raising blood calcium, but this has since been disproved by Harris.

The availability now of vitamin D concentrates with an activity 10,000 to 300,000 times that of cod liver oil makes possible the production of a hypervitaminosis D or a toxic condition. By giving one-tenth cubic centimeter of the 10,000× concentrate, the blood calcium of an animal may be raised to fatal limits, 20-25 milligrams per 100 cc. of blood. This causes hemorrhage from intestines and stomach, anorexia, coma and death.

It is found in such conditions that the absorption of calcium is increased both from the bones and intestine and that normal excretion by way of the intestine is prevented.

Tests with smaller amounts of viosterol which do not produce death show that with an increased calcium in the blood and a decreased deposition in the bones, there is an increased tendency to deposit calcium in the blood vessels, kidneys, muscles and other soft tissues of the body.

Due to the removal of freshly deposited calcium phosphate from the bones which these potent solutions of viosterol are able to bring about, rather large amounts of vitamin D have been used lately in arthritis with good results. This large amount of the vitamin removes the calcium phosphate that has been newly laid down in arthritic deposits.

Vitamin E, the third of the fat soluble vitamins, was originally found in wheat germ oil, by Evans. Evans and his assistants were studying the oestrus cycle in rats and found that the cycle varied markedly with changes in the diet. They attempted to put their experimental rats on a standard, simplified diet and used the diet which at that time was believed to be a perfect simplified diet. On this diet the rats did not show any oestrus changes at all, nor did they until green vegetables or wheat germ oil was added to the diet.

Further studies by Evans and his group showed that the active principle is in the non-saponifiable fraction of the oil, and to be an inert fraction distilling at 200-230° C. at a pressure of 5 mg. The most highly purified preparations were found to be very inert, resisting oxidation, solution in concentrated acids or alkalies as well as reduction and heat.

The lack of this vitamin as shown by Evans gives rise in the female to a continuous desquamation or removal of the epithelial cells which line the uterus. Eventually this lining will be eroded away until nothing remains but the underlying connective tissue, and when this occurs, the animal becomes sterile through inability of the fertilized egg to find a place to grow. However, the fetus in vitamin E deficiencies not as severe as this, may grow until the sixteenth or seventeenth day of the twenty-one-day gestation period and then die. However, even in severe deficiencies of vitamin E sterility in the female, fertility may be regained on again giving plenty of E vitamin.

In the male, however, the lack of E vitamin brings about in time complete and permanent sterility by causing a desquamation and loss of immature sperm cells. Sure has found that the successful rearing of young is depend-

ent on the amount of vitamin E and also of vitamin B in the mother's diet, and that the successful production of milk is dependent on these factors.

Verzar has shown that E vitamin acts very much in the body as though it stimulated the action of the anterior lobe of the pituitary body. He has shown that by giving vitamin E concentrates to a young virgin rat, he is able to bring about hypertrophy of the uterus. Verzar has also shown that in the absence of E vitamin the infantile, silky character of the rat's hair persists into adult life.

It is evident that this vitamin is concerned with other tissues than those strictly confined to the function of reproduction. It is believed that it has a stabilizing function on such easily irritated tissues as the skin, mucus surfaces and linings of the body and the germ plasm. In this line it is interesting to note that it has been used successfully in stubborn cases of eczema.

Vitamin E is found in largest quantities and concentration in wheat germ oil, to some extent in crude cottonseed oil and corn oil, but is lowered in activity in these oils by the refining process. It is found in butter but not in lard or in cod liver oil. In the animal body it is found in muscle and fat and uot in the liver or kidney where vitamins A and D are found. It is found in green leaves, and lettuce is an excellent source of this vitamin both in the leaf and in the seed.

In these three vitamins we have exceedingly interesting substances, which are intimately concerned not only in the well-being of the individual but in the maintenance of life itself. These vitamins are normal constituents of the natural oils and fats as a component of that biologically interesting group of substances called the non-saponifiable matter.

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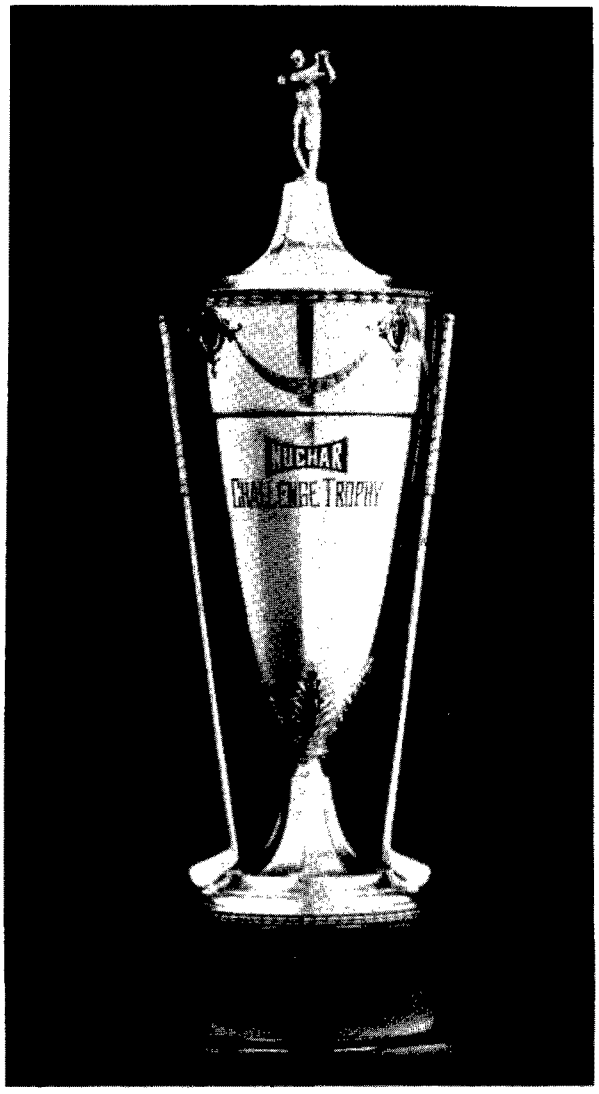

Annual Golf Tournament

THIS event, which has become a classic, widely known throughout all technical circles, promises to be the best golf tournament yet held, because of the appointment of Mr. Albert F. Sanchez chairman of the committee by President Harris. Being right on the ground, Mr. Sanchez is better able to provide for a fine tournament than out of town chairmen have been in the past, and it is understood that with the coöperation of Mr. Ganucheau and the title holder, Prof. Williamson, this annual event is something to look forward to.

Present plans call for play to start at the Metaire Country Club as soon after noon as possible, and the entire membership is familiar with this course and knows that it is one of the sportiest and best courses in the country, so prepare to enjoy yourself on Thursday afternoon, as usual.

C. S. Williamson
1933 *Champion*