EARLY EXPERIENCES WITH FISH OILS -- A RETROSPECT

By Charles E. Bills*

Because of the interest in the property of fish oils, this article is being reprinted in this periodical since we feel it contains some interesting observations regarding the properties of various fish oils.

The Editors

I was fortunate in having my last year of graduate work under Professor E. V. McCollum. This was shortly after his group discovered vitamin D in cod-liver oil and just before Steenbock and Hess associated D with ultraviolet light and the sterols. My thesis dealt with the occurrence and properties of the new vitamin and some improvements on McCollum's line test for measuring it. It included the finding that a fish body oil (menhaden) is, like the liver oils, a source of vitamin D.

One of the visitors at Johns Hopkins in early 1924 was E. Mead Johnson, Jr., the baby-food manufacturer, who had it in mind to remove cod-liver oil from the folk medicine category and to promote it on its merits. We met in the rattery, and, after a few days of deliberation, I agreed to organize a research laboratory for his company at which fish oils should receive further study. I sketched some floor plans, and the architect and builder went to work.

Johnson and I spent six weeks of the summer in Newfoundland, touring the fisheries and learning what we could about the habits of cod and the production of oil. There we met Jack Drummond, who had come over from London on a similar mission. Drummond was interested to hear more about McCollum's new vitamin, and gave us in exchange much information about the fishing industry. He had recently traced the vitamin A of fish livers to a possible origin in phytoplankton, and he surmised that the vitamin D had a similar lineage, i.e., plankton — little fish — big fish. In view of this I gave particular attention to the collecting of capelin and squid, principal foods of the cod in Newfoundland waters. We made oils from these and a few other species that were fat enough to yield oil by simple rendering. The samples were to be our first study material at the new laboratory.

Delays in construction enabled me to have some additional months in Baltimore, until the end of 1924. This struck me as an opportunity to isolate a specimen of vitamin D from the ample supplies of cod-liver oil now available. I learned that Lawson Wilkins, a young pediatrician with whom I shared laboratory space, was bent on the same accomplishment, and, as we were both in a hurry, we joined forces. We got as far as attempting to fractionate the unsaponifiables in a newly-improved vacuum still put at our disposal by Colonel E. B. Vedder. At this point the vitamin vanished. Years later, when Brockmann did isolate vitamin D from tuna-liver oil, I could better appreciate his achievement. His starting material was hundreds of times more potent than ours, and his principal technique, chromatographic adsorption, was in our day only a botanist's lecture aid.

Professor McCollum contributed to the Mead Johnson laboratory a breeding stock of rats, descendants of those with which he discovered vitamins A and D. The genealogy of this distinguished line deserves mention. Originally assembled for genetic studies, the strain was a mixture of albinos, Irish blacks, and a wild buff sport from the Liverpool docks. Under McCollum at Wisconsin, they were probably the first rats ever to be used in nutritional research. I in turn supplied a branch of the family to Windaus and Holtz at Gottingen and to laboratories elsewhere.

The Evansville laboratory was ready on January 1, 1925. My first assistant was F. G. McDonald, recently graduated from Purdue. During the previous fall he

* Consultant, Baltimore, Md.

Note: This article appeared in Nutrition Reviews, vol. 13, no. 3 (March 1955), and is being reprinted with the permission of the editors of that periodical and the author.

had built up the rat colony to useful size, and we now began 25 years of work together. From the start it was evident that our efforts would be divided between fish oils and irradiation products, not to mention other fields of nutrition with which the company was concerned.

During 1925 and 1926 we examined a number of oils and fats besides the specimens collected in Newfoundland. We were chiefly interested in vitamin D, and at first paid only incidental attention to the better known vitamin A. Some of this work was planned to broaden our knowledge of the occurrence of vitamin D. Some was directed at the problem of origin. Some was primarily quality control on cod-liver oil. The control work required an inordinate number of rats, but it gave us valuable experience and data from which we built a quantitative procedure out of what formerly had been a pass-or-fail test.

Our first published survey included assays on the oils of 17 marine species. It fairly well established the concept that fish oils are the natural source par excellence of vitamin D. It covered three new body oils (herring, salmon, and sardine) besides the original menhaden oil, each of which was comparable to cod-liver oil as a source of vitamin D. We never could make these body oils palatable enough for human use, but the poultry feed people soon developed a great market for them, especially for sardine oil. This was fortunate, for it released more cod-liver oil to human consumption at a time when it was almost the only source of medicinal vitamin D.

The survey included all the marine oils then produced in quantity, but it gave no encouragement to a search for others. Three of the oils were equal to cod-liver oil, but the only one that was superior was Hess' pufferfish, a curiosity commercially unavailable. Consequently we did little with fish oils from 1927 to 1932, switching to more promising fields, especially the development of synthetic vitamin D. During this period, however, we collaborated with Hess in a study of individual cod livers which brought out the surprising fact that the potency of the oil varies inversely with the fatness of the liver. This was the first intimation that those species of fish which regularly have lean livers may nevertheless be excellent vitamin sources.

In 1931 the Health Organization of the League of Nations held a conference in London to establish international standards for the vitamins. My assignment was to prepare the definition of the vitamin D unit. At this time I again met Drummond and learned that halibut-liver oil exhibits an exceptional vitamin A potency, although the yield of oil is small in comparison with cod. It now seemed in order to take another look at the lean-liver species, and so the program was revived, this time with a strictly Edisonian approach designed to include every fish of major commercial importance.

Our laboratory staff had grown considerably, and was now enlarged for this undertaking. J. C. Wallenmeyer was the procurement man who visited the fisheries on both coasts and arranged for agents in Japan (our principal source), the Philippines,, and southern hemisphere. He devised an extraction process in which liver was liquefied by alkalinizing to a critical pH and the oil recovered centrifugally. Thus it became possible to recover vitamins from the leanest livers, and by scrubbing the aqueous phase with cod-liver oil a high degree of efficiency was realized. Wallenmeyer and I built a vitamin A spectrophotometer which saved countless hours of animal work.

The program got under way early in 1932, and by 1934 we had data on more than 100 species. European workers had noted an interesting correlation between zoologic order and vitamin storage in liver, namely, that the cartilaginous fishes (sharks, etc.) store little vitamin D. We confirmed this, and found several new relationships. The flatfishes (halibuts, soles) were rich in vitamin A; good to poor in D. The rockfishes were mostly superior sources of both vitamins. The cod fishes, in comparison

with most other groups, were only mediocre sources of vitamin D. But above all were the percomorphs (tunas, basses, etc.), most of which carried extraordinary concentrations of vitamins D and A, even hundreds of times more than the cod.

It was obvious that by blending the liver oils of certain percomorph fishes we would have a product of considerable appeal to our physician-customers. But what to call such a product, briefly and definitively without resort to a trade name? Sensing the penchant of doctors for classical terminology, I wanted something reminiscent of Oleum Morrhuae. The local Latin teacher came up with "Oleum Percomorphum," a name which probably contributed much to the commercial success of the product.

Only those in the pharmaceutical business can appreciate the problems which beset a new product. To illustrate: A physician wrote to inquire if "O. P.," used as a food adjunct, is kosher, i.e., if all the species involved are fishes with scales. He knew that one of the component species is endowed with scales when young but loses them at maturity--what, then, is the status? The answer, according to the highest rabbinical authority, was that once a fish is kosher, it so remains.

The fishermen of the world soon had a bonanza. Livers formerly regarded as offal were in such demand that in some species they sold for more than the rest of the fish. The highest price that I recall was $8 a pound for frozen ishinagi liver, the tonnage of which was rather limited. Each species had its price, which we revised from time to time on the basis of assays and oil yield. Our problem now was to dissuade the fishermen from palming off worthless livers for the desired ones. Happily, we soon discovered that a good way to recognize a fish is by its liver. The shape, color, markings, relative size of lobes, and pattern of venules are highly specific, and by these criteria one can differentiate species that are confusingly similar in external appearance. A set of preserved liver standards was used to train our inspectors, who could then sort quantities of freshly thawed material at a glance. This method of distinguishing species is still in use by some of the fish and game authorities.

The percomorph liver oils richest in vitamin D are those from the various tuna species. In 1934 we assayed one of these by Massengale's rat-chick method, and were thereby able to demonstrate the existence of more than one form of vitamin D in nature. Later, when Brockmann isolated vitamin D from tuna-liver oil, it proved to be a mixture of D_2 and D_3.

We never could show how the fish gets its vitamin D. The capelin and squid oils from Newfoundland did not account for the vitamin in the cod. Some catfish that we raised in captivity without a source of vitamin D seemed to accumulate as much as though they had received it, which would point to a synthesis. But some cod that we dosed with ergosterol, and cod livers digested with ergosterol, showed no synthesis. The question is still open.

Synthetic vitamin A has in recent years joined D_2 and D_3 in competition with fish oils, but fishing is an old art likely to continue, and the fish oils which we explored in 1924-1934 will serve in nutrition for a long time.