

The conclusion may be drawn that the changes in the different constituents of the blood are not proportionate inasmuch as the protein concentration generally increases more than either the total electrolytes, the total dissolved substances or the hemoglobin. Concerning the relation between the hemoglobin and the serum protein change, it must be remembered that if the water-loss comes from the serum, which is roughly 50 per cent of the blood, then the increase in serum protein should be double the increase in hemoglobin; this is very nearly true in our average figures (6.1 and 2.9). It is also evident that the degree of concentration occurring as a result of the bake, if measured by the change in serum protein content, tends to be larger the lower the initial serum protein content. The fluid lost from the serum in excess of that gained from the tissues appears to be a salt solution of lower concentration than the serum.

70 (2302)

Studies on the chemistry of cod liver oil.*

I. The effect of hydrogenation upon the vitamine content.

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A survey of the literature reveals comparatively little on the hydrogenation of cod liver oil. Drummond,¹ working with whale oil, hydrogenated at 250° C. for 4 to 6 hours, found that the hardened oil was entirely deficient in "fat-soluble A," which at that time was generally also regarded as the "antirachitic vitamin". Since then the bulk of evidence has tended to show that

*This investigation was started in January, 1922, and is still being continued.

¹ Drummond, J. C., *Biochem. J.*, 1919, xiii, 81.

"fat-soluble A"—the antiophthalmic, growth-promoting vitamin—is not identical with the antirachitic vitamin.

Paal and Roth,² studying the catalytic action of colloidal metals of the platinum group, hydrogenated cod liver oil and butter. The process used by these investigators is a very mild one. As modified to suit our needs, it is carried out at about 55° C. for a period of about 36 hours. This is in sharp contrast to the drastic hydrogenation reported by Drummond.

Employing both the curative and preventive type of experiment the various fractions obtained by us, and about to be described, were tested on more than 150 rats. The diets used included a synthetic diet practically free from antirachitic vitamin, the McCollum diet No. 3143 and the Pappenheimer-Zucker diet D.

Fraction I.—This fraction, which possesses no vitamin activity, is the concentrated water reduction mother-liquor.

Fraction II.—The hydrogenated cod liver oil, obtained as a snow-white product, is odorless and tasteless, and melts at about 55° C. The yield is about 95 gm. from 100 gm. cod liver oil. When used in amounts corresponding to 0.100 gm. cod liver oil daily, it prevents and cures rickets. Smaller dosage was not tried.

Fraction III.—The residue left after extracting fraction II with alcohol. The yield is about 90 gm. from 95 gm. of fraction II. Fraction III is inactive in amounts corresponding to 0.250 gm. cod liver oil daily. Larger doses were not tried.

Fraction IV.—A creamy-white substance, almost odorless and tasteless, melting at about 30° C., extracted from fraction II by means of alcohol. The yield is about 4.5 gm. from 95 gm. fraction II. When given in amounts equivalent to 0.100 gm. cod liver oil daily, it prevents and cures rickets. Smaller dosage was not tried.

Fraction IVa.—This is the same as fraction IV, resembling it in appearance, but with the cholesterol removed. Yield is about 0.045 gm. from 4.5 gm. fraction IV. Administered in amounts corresponding to 0.250 gm. cod liver oil daily, it prevents and cures rickets. Smaller dosage was not tried.

Fraction C.—The cholesterol fraction proved to be inactive.

In the few cases in which the above active fractions were tested in attempts to cure ophthalmia, unsatisfactory results were

² Paal, C., and Roth, K., *Ber. chem. Ges.*, 1908, xli, 2282; 1909, xlii, 1541.

obtained. However, we do not conclude that hydrogenation destroys the antiophthalmic vitamine, inasmuch as growth is a better index than ophthalmia, and our animals grew fairly well.

In this connection, it is of interest to note that Goldblatt and Zilva,³ using the preventive type of experiment with animals fed on the McCollum diet No. 3143, found that 33.7 mg. daily of a hardened cod liver oil protected against rickets, and that 1.8 mg. promoted growth. The original oil, before hardening, also promoted growth in daily doses of 1.8 mg. The anti-rachitic value of the original oil was not determined.

From the above, it appears that the vitamine potency of cod liver oil is not appreciably destroyed by a suitable hydrogenation process.

It is thus possible to prepare a potent concentrate which may be used as a starting point for further chemical fractionation, and as a source of vitamine possessing obvious advantages over cod liver oil. Further work along this line is in progress and detailed data will appear in an early publication.

71 (2303)

The occurrence of gastric lesions in rats, and their possible relation to dietary deficiency.

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In examining the gastro-intestinal tract of rats which were being used for other experiments our attention was directed to the frequent occurrence of lesions in the rumen or esophageal portion of the stomach. These lesions, in brief, consisted of an inflammatory edema of the mucosa and submucosa, with marked cellular reaction, and in most cases, localized ulceration. Associated with these inflammatory changes there was always present more or less epithelial hyperplasia. These lesions were

³ Goldblatt, H., and Zilva, S. S., *Lancet*, 1923, ii, 647.