

Chemistry. — *Researches on fat metabolism X*¹⁾. *Feeding experiments on dogs with simple saturated triglycerides.* By P. E. VERKADE, J. VAN DER LEE and A. J. S. VAN ALPHEN.

(Communicated at the meeting of April 24, 1937).

§ 1. VERKADE and VAN DER LEE²⁾ have shown that administration of different saturated triglycerides, each containing only one component acid, to one and the same healthy subject under as far as possible the same conditions gives rise to the excretion of dicarboxylic acid in the urine to a very different degree. A comparative survey of the diacidogenic properties of the triglycerides investigated *with regard to the human organism* looks as follows:

tricaprylin	weakly	diacidogenic
trinonylin	fairly weakly	„
tricaprin	strongly	„
triundecylin	strongly	„
trilaurin	practically not	„
tritridecylin	not	„

Some time ago FLASCHENTRAEGER and BERNHARD³⁾ published data concerning similar experiments on dogs with sodium salts and with methyl and ethyl esters of saturated fatty acids. The drawing of conclusions from these data is hampered to some extent by the fact that these workers did not administer all the compounds of a homologous series to the same dog; it is not likely that all test-animals tended to dioic acid-acidosis and diaciduria to the same degree. Excretion of dicarboxylic acid in the urine was only noticed with the sodium salts and with esters of caproic acid, nonoic acid and capric acid; the amount of dicarboxylic acid was always considerably greater with the salt and the esters of capric acid than with the salts and esters of both other acids.

Similar experiments with sodium salts of fatty acids had already been announced in our second paper on fat metabolism⁴⁾ and at the time of the appearance of the first of FLASCHENTRAEGER and BERNHARD's papers quoted above³⁾ were in fact in progress. It has seemed to us that under the given circumstances it was best to stop our experiments in this direction. It may be stated here — in agreement with the results obtained by the above

¹⁾ For tactical reasons this paper is made to precede the papers VIII and IX already announced.

²⁾ Biochem. J. 28, 31 (1934).

³⁾ Z. physiol. Chem. 238, 221 (1936); comp. also Helv. chim. acta 18, 962 (1935).

⁴⁾ Proc. Royal Acad. Amsterdam, 36, 314 (1933) (Febr. 25, 1933).

mentioned workers — that administration of sodium undecate to the dog T. in an amount of about 1.3 g per kg of body weight per day for 4 days did not give rise to excretion of undecanedioic acid in the urine.

Experiments commenced at the same time on dogs with simple saturated triglycerides have, however, been continued. The results of this work are discussed in this paper.

§ 2. The healthy adult dog T. (about 12 kg, ♂); after two preceding fast-days, was given 50 g of the triglyceride to be investigated (about 4 g per kg of body weight per day) in three equal portions, always at the same time and each time as an addition to a meal which consisted generally of as far as possible equal amounts of boiled potatoes (20–30 g) and lean horse meat (80–100 g). Water was supplied as desired. The urine passed during the day of the experiment and some succeeding days was collected and tested for the presence of higher dicarboxylic acids. Data have been furnished to a sufficient extent in previous papers⁵⁾ concerning the method of working up the urine.

An adequate interval of time was always allowed between the various experiments and during this the test-dog could resume its normal mode of life. At least two experiments were made with each of the triglycerides investigated (triheptylin-triundecylin); these always furnished qualitatively similar results. Disturbances in the experiments through vomiting, diarrhoea etc. did not occur.

§ 3. It was only after administration of *tricaprylin* that an appreciable amount of dicarboxylic acid, actually the ω -oxidation product of the component acid (C_8), was found to be present in the urine; we succeeded in isolating therefrom 0.16 g and 0.11 g of suberic acid respectively in two experiments. After administration of *trinonylin* and *tricaprin* the urine contained generally a very small amount of the corresponding ω -oxidation product (C_9 or C_{10}); some mg of azelaic acid or sebacic acid could be isolated in these cases. The experiments with *triheptylin* and *triundecylin* always gave negative results.

The results of these experiments with simple triglycerides thus fit perfectly with those of the above described experiments of FLASCHENTRAEGER and BERNHARD with the corresponding sodium salts and esters. For this reason we have considered it unnecessary to repeat the feeding experiments with triglycerides with other dogs. We believe we can say with certainty that a comparative survey of the diacidogenic properties of the triglycerides investigated *with respect to the dog* must look as follows:

triheptylin	not	diacidogenic
tricaprylin	weakly	"
trinonylin	practically not	"
tricaprin	practically not	"
triundecylin	not	"

The difference between this table and that given at the beginning of this paper is indeed very striking; the variation of the diacidogenic properties

⁵⁾ Comp. VERKADE and VAN DER LEE, Z. physiol. Chem. 227, 215 (1934); VERKADE, VAN DER LEE, VAN ALPHEN and ELZAS, Proc. Royal Acad. Amsterdam, 38, 945 (1935).

of the simple saturated triglycerides with rise in the homologous series is quite different with man than with the dog. It would serve no object to theorize on the cause of this difference here.

From our experiments and those of FLASCHENTRAEGER and BERNHARD it may indeed be concluded that the dog has little tendency to dioic acid-acidosis and diaciduria. One may be reminded here that it is very difficult to produce ketonuria in healthy dogs⁶⁾. In our opinion the two phenomena are related and to be expected with the carnivores in general. We are here touching the connection between carbohydrate metabolism and fat metabolism, which appears in a new light after our discovery of the degradation of fatty acids by ω -oxidation and subsequent bilateral β -oxidation and will be discussed in later communications from our laboratory.

The fact that the results of our experiments with simple triglycerides agree qualitatively completely with those of the experiments carried out by FLASCHENTRAEGER and BERNHARD³⁾ with the sodium salts of the corresponding fatty acids, is a proof of the view that the observed differences in the diacidogenic properties of the triglycerides are not caused, or at least not to an appreciable extent, by differences in the velocity with which these substances are hydrolysed in the intestine. Although we have never postulated anything of the kind, one ought a priori to take this possibility into account. It is for this reason, among others, that comparative investigations have been made in our laboratory on the velocity of saponification of a series of simple triglycerides under the influence of pancreatic lipase; we will here merely refer to this work which has only been published in part as yet⁷⁾.

This parallelism in the behaviour of the triglycerides and the corresponding sodium salts is obviously likewise contradictory to the hypothesis, put forward at the time by FLASCHENTRAEGER, BERNHARD, LOEWENBERG and SCHLAEPFER⁸⁾ that ω -oxidation only occurs with glycerides resorbed as such, i.e. without preceding saponification. We need not go into the matter here as this opinion is not maintained in latter communications from FLASCHENTRAEGER and his co-workers.

We wish to thank the VAN 'T HOFF-Fund and the HOOGEWERFF-Fund for assistance in carrying out this work.

Rotterdam, March 1937.

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⁶⁾ Comp. e.g. VON NOORDEN and ISAAC, Die Zuckerkrankheit und ihre Behandlung, 8th impr., 1927, p. 184.

⁷⁾ HOLWERDA, VERKADE and DE WILLIGEN, Rec. trav. chim. 55, 43 (1936); 56, 382 (1937).

⁸⁾ Z. physiol. Chem. 225, 157 (1934).