EXPERIMENTAL MODEL FOR TYPE 2 DIABETES

THE HIGH-FAT ANHYDROUS BUTTER DIET

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We compared high-fat diets in order to determine which was the most effective in inducing an obese/diabetic phenotype.

Laboratory mice [Janvier-labs in St Berthevin (53)] fed on version 19 of the U8978 High Fat ("HF") Anhydrous Butter diet formulated by SAFE, from the age of 10 weeks, when compared to animals subjected to the standard A03 diet, present very marked phenotypic characteristics. Effectively, in the course of time, the "HF" animals' weight quickly gained over that of the A03 mice (Figure 1A). In addition, the blood sugar levels measured greatly increased in the "HF"s when compared to the control group mice (Figure 1B).

Furthermore, after 12 weeks of the diet, the size and appearance of the liver as well as the fat in the mice's epididymis corresponded to the sort of metabolic disturbances to be expected (Table 1). By comparison, those animals that were put under the 230 high-fat Purified Diet still benefited from a weight gain, whereas the variation in their blood sugar levels was lower (+14%). What is more, a high level of reproducibility between the animal groups subjected to "HF" or A03 diets was obtained at the moment of performing functional tests into glucose and insulin tolerance (Figure 2). This anhydrous butter diet does, then, induce obesity as well as phenotypic anomalies comparable to type 2 diabetes.

Lastly, the low variability in biological characteristics obtained through this "HF" diet has allowed us to retain all the animals for the study, without exclusion. This last point is of importance, since it makes it all the more possible for us to meet the ethical requirements of the research programme. Beside this, this particular diet has real practical advantages. Effectively, to provide a high-fat diet, it is pressed into granulated form and keeps a good consistency in animal laboratory conditions (temperature, humidity, etc.). It is, moreover, well-adapted for tests in metabolic cages.

SAFE's HF anhydrous butter diet is, in conclusion, a reliable tool, which has allowed us to reach important preliminary findings in the framework of our research programme into the role played by a new neuropeptide involved in regulating carbohydrate metabolism and behavioural patterns in eating.

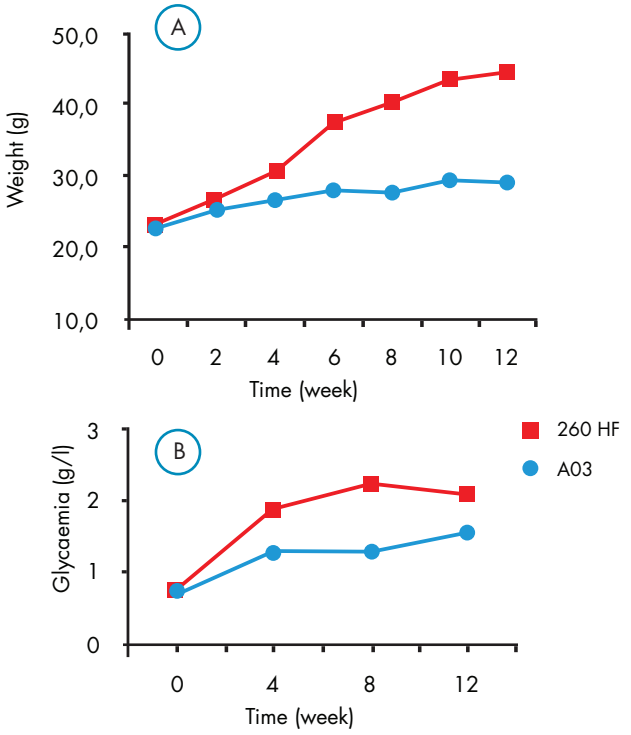

Figure 1:
Effect of High Fat anhydrous butter diet changes in weight and glycaemia in aged mice from 10 to 22 weeks compared to animals subjected to the standard A03 diet.

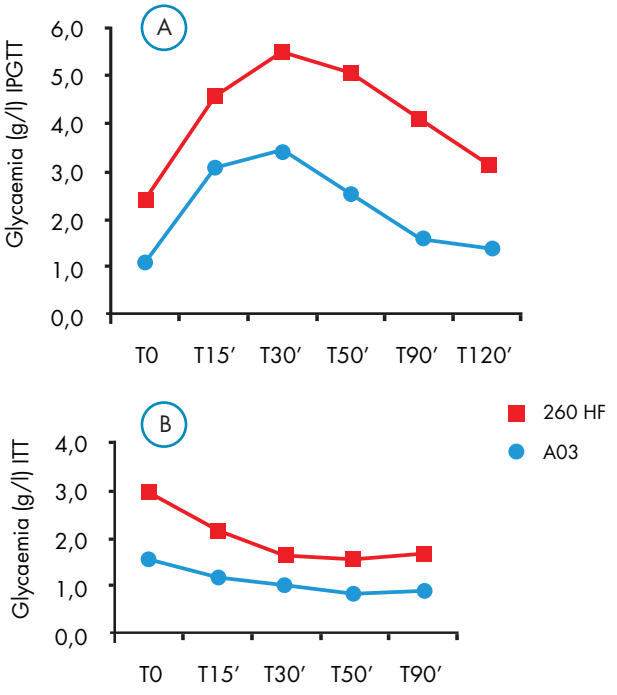

Figure 2:
Functional tests performed during the light period on mice fasted 12 or 6 o'clock. The glucose tolerance test (IPGTT) is standardized by an ip injection of 1.5 g glucose / kg. The insulin tolerance test (ITT) is performed by an ip injection of 0.75U insulin.

MICE C57BL6/J N=10 PER DIET	*ANIMAL WEIGHT (g)*	*GLYCAEMIA (g/l) AFTER 12H FASTING*	*LIVER WEIGHT (g)*	*FAT MASS OF EPIDIDYMIA (g)*
A03	29.36 ± 0.47	1.16 ± 0.05	1.00 ± 0.04	0.33 ± 0.04
260 HF	44.18 ± 0.70	2.11 ± 0.06	2.62 ± 0.14	1.43 ± 0.04