

Pharmacological Research in Great Britain.

THE second Annual Report of the Pharmacological Laboratories of the Pharmaceutical Society of Great Britain (1927) gives a brief summary of the research work carried out during the year, and indicates the part the laboratory is beginning to play in the physiological standardisation of different drugs for commercial manufacturers. In February of last year the Vitamin-testing Department, under Dr. Katharine H. Coward, was ready to carry out its first tests, and these now occupy an important place in the laboratory's work.

The director, Dr. J. H. Burn, has continued his researches on the metabolism of rats on a fat diet: he has found that in summer the excretion of acetone bodies in the urine of a 100-150 gm. rat reaches a maximum of 50 mgm. in a day, whilst in winter the maximum may not be greater than 5 mgm. The summer acetonuria can be inhibited by injection of pituitary extract or adrenalin, indicating that these hormones control the metabolism of fat as well as that of carbohydrate. On the other hand, daily injections of insulin, after a day or two, increase the winter acetonuria, and this increase is not simply related to the fall in the blood-sugar, since the latter occurs to about the same extent on all days on which the injections are given.

Some work has been carried out on the assay and preparation of extracts of ergot, and also, in conjunction with Mr. A. Bourne, on the clinical value of pituitary and ergot extracts. It was found that during labour a dose of 2 units of pituitary extract was quite sufficient to hasten its conclusion, and also that of the possibly active substances present in extracts of ergot, the specific alkaloid ergotoxine or ergotamine produces, after a short latent period, a

prolonged contraction of the uterus *postpartum*, whilst histamine causes an immediate powerful but short-lived contraction, and tyramine is inert.

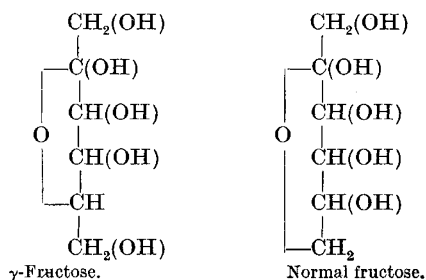
A paper on the oestrus-producing hormone has been published by Drs. Burn and Coward: it was found that the individual variation between different rats or different mice is as much as 1000 per cent. The authors therefore define the unit as the dose necessary to produce oestrus in 50 per cent. of ovariectomised animals. They have constructed a standard curve relating the percentage of rats in which oestrus occurs to the dose injected from observations on a group of 90 animals. A curious point that emerged from this work was that the mouse unit has exactly the same value as the rat unit, in spite of the difference in body weight between the two species.

In the vitamin department, a stock colony of Wistar rats is in process of being built up, by in-breeding the animals and maintaining them on a constant diet: the most suitable diet, however, has not yet been determined. A sample of irradiated ergosterol is being used as a standard for vitamin D assay: a unit has been defined as the amount of antirachitic activity contained in 0.0001 mgm. of this sample. This definition has been rendered necessary by the fact that certain workers are defining the unit of vitamin D as the least amount which will cure rats of rickets, when they are maintained on a rachitogenic diet: such a unit may vary by 400 to 500 per cent. in different experiments. It is hoped to use a sample of the unsaponifiable matter of cod-liver oil as a standard for vitamin A in the near future. The report also gives the number of samples of the different preparations which have been assayed during the year: approximately 170 were tested.

The Synthesis of Cane Sugar.¹

By Prof. AMÉ PICTET and H. VOGEL.

THE fine researches of Haworth and of Irvine have shown that fructose (levulose) does not possess the same chemical composition when it is in one of its natural combinations (cane sugar, inulin) as when it has been extracted. Hence it must be admitted that it can exist in two isomeric forms, one of which, to which the name of γ -fructose has been given, is unstable and changes spontaneously into the other, called normal fructose, as soon as it is set free. Haworth and his collaborators have made it very probable that the formulæ which should be attributed to these two forms are the following:



It follows from these facts that if it is attempted to realise a synthesis of saccharose by the union of its two constituents, glucose and fructose, it cannot be effected by utilising the second of these sugars in its normal form, the only one available. It would

be necessary to start with one of the artificial derivatives in which it occurs in the γ form. Some of these are known (methyl, ethyl), but none of these would be available for the operation in question, since the substituted groups that they contain are too firmly fixed to the rest of the molecule to permit of their being detached, once the condensation with the glucose had been carried out.

Hence the synthesis of saccharose necessitates the preliminary preparation of a derivative of γ -fructose containing only substituent groups relatively easy to remove. The following observation has furnished us with a substance which fulfils this condition.

We have found that when the tetracetate of normal fructose is prepared by the method of Hudson and Brauns (*Jour. Amer. Chem. Soc.*, **37**, p. 2739; 1915), that is, by treating fructose at a low temperature with acetic anhydride and zinc chloride, on crystallising the product from alcohol, a second compound is formed in small quantity which remains in the mother liquors. On evaporating these in a vacuum a thick syrup is obtained which, on contact with cold water, is slowly converted into a solid vitreous mass. Up to the present, this substance has not been obtained in the crystalline condition, but its analysis, and the fact that it easily reduces alkaline copper solutions, proves that it consists of a second tetracetate. Moreover, its rotatory power, much lower than that of the normal tetracetate, would suggest that it belongs to the γ series.

The formation of a derivative of this nature would be explained by admitting (as already suspected by

¹ Translated from *Comptes rendus* for Mar. 19 of the Paris Academy of Sciences.