Nuclear Histone from Bird Erythrocytes in the Preparation of Insoluble Insulin Compounds

FOLLOWING early work done in these laboratories on the use of thymus histone for the preparation of a histone-zinc-insulin with prolonged hypoglycæmic activity[1], we have now tried a histone from the nucleus of bird erythrocytes.

Drs. Lajmanovich and Mittelman directed our attention to this protein; it is usually classified as a histone, but they found in some reactions that it shows some properties of the protamines. We thank them for preparing the histone we employed, from turkey erythrocytes, by a modification of the method of Kossel[2].

A suspension of histone-zinc-insulin (histone from erythrocytes), at *p*H 6·8, and containing 40 I.U. insulin per c.c., was prepared by the usual procedure.

When administered to diabetic dogs, a fall in the blood glucose took place that lasted for a little more than twenty-four hours, when the initial glycæmic value was again obtained.

The type of glycæmic curve (glycæmia-hours) was similar to that obtained when the same amount of protamine-zinc-insulin (protamine-salmin) was administered. The hypoglycæmic action of the same amount of histone-zinc-insulin (thymus histone) was never so prolonged.

In conclusion, it can be stated that the histone-zinc-insulin complex prepared with histone from the nucleus of turkey erythrocytes has a hypoglycæmic activity more like that of protamine-zinc-insulin than that of the thymus histone-zinc-insulin preparation.

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Buenos Aires. Nov. 6.

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Detection of Chemotherapeutics in Thin Sections of Tissue by the Aid of Fluorescence Microscopy

IT has long been known that, thanks to their property of showing fluorescence in ultra-violet light, certain substances can be demonstrated even in very low concentrations. As a large number of the common drugs show fluorescence, it would appear reasonable to endeavour to demonstrate their presence also in tissues by the aid of fluorescence microscopy. The method has not been used very greatly, however, in view of the fact that the natural fluorescence of the tissues is so strongly blue that it masks the fluorescence of the drugs administered. In addition, the histological methods used have not excluded the possibility of changes in the locality and concentration of the substance sought during the actual preparation.

I have therefore adopted Altmann-Gersh's freezing-drying method for fixing and drying the sections, in doing which I have made use of a modification which has recently been described in detail by F. Sjöstrand[1]. The principle is as follows. The organs and pieces of tissue to be studied are removed and immediately frozen in liquid air. They are then dried over phosphorus pentoxide *in vacuo* in a refrigerator at about − 40° C. They are embedded in paraffin and cut into histological sections, which are mounted on slides, and are then ready for microscopical examination.

Drugs of which the fluorescence colour is other than blue can be demonstrated directly in the sections. For example, Prontosil rubrum and soluble, which have a strong red fluorescence, can be demonstrated[2] even in a concentration of $1 \times 10^{-10}\,\gamma$ per μ^3, which is a considerably greater sensitivity than that obtained by observing the natural colour in an ordinary light microscope.

Drugs with blue fluorescence can frequently be made to change their fluorescence colour by heating in a small electric oven to different temperatures for different lengths of time. Sulphathiazole, for example, turns yellow on being heated to 170° C. for 5 minutes, the tissue itself remaining blue. This produces a beautiful contrast, allowing of the location of sulphathiazole in tissues and cells. In an ordinary light microscope, no traces of sulphathiazole can be discovered in such sections, any more than is possible in a fluorescence microscope before heating.

By the aid of this method it is possible to demonstrate the presence of a number of drugs, for example, sulphanilamide, sulphapyridine, papaverine, inulin (yellow after 3 min. at 200° C., the tissues still being blue), etc. Penicillin, which has a green fluorescence, can be identified without difficulty in muscle after an intramuscular injection and after the sections have been heated to 175° C. for 5 min.; the penicillin is then yellow-brown. In some cases the contrasts are obtained by the substance sought keeping its colour, while the tissues change their fluorescence colour. Sodium salicylate, which has a blue fluorescence, can thus be demonstrated at 200° C. after 5 min., the tissues at that temperature being yellow.

As the natural fluorescence is considerably differentiated, no special staining is necessary to facilitate the identification of the tissues.

By the aid of this method it has proved possible to study in detail the location of chemotherapeutic substances in tissues and their secretion.

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Detection and Determination of Traces of Methyl Bromide

METHYL bromide has many advantages as a fumigant, but suffers from the disadvantage that, over a range of concentrations liable to be encountered during airing, it is harmful to man and not detectable by smell.

The current method of detection, which does not serve for determination, depends on the appearance of a green 'copper' colour in the flame of a Halide detector lamp. This method is, of course, not specific to bromide and is inconvenient under many practical