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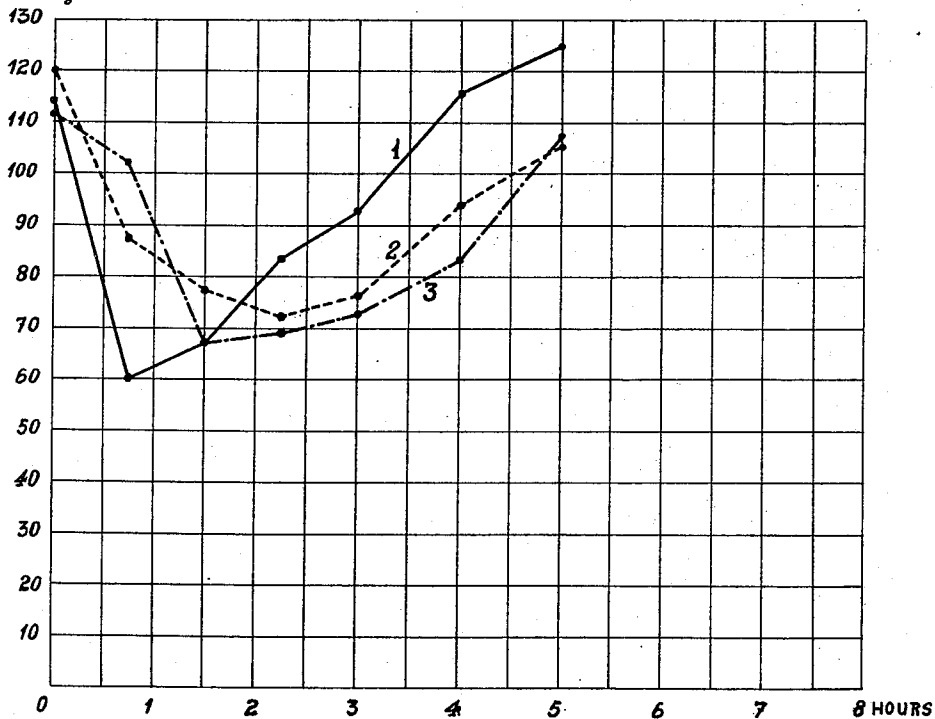
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2,294,016

INSULIN AND PECTIN SOLUTION FOR INJECTION PURPOSES

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BLOOD SUGAR
IN mg PER 100 c.c.



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UNITED STATES PATENT OFFICE

2,294,016

INSULIN AND PECTIN SOLUTION FOR
INJECTION PURPOSES

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6 Claims. (Cl. 167-75)

The invention relates to insulin solutions which are administered by subcutaneous, intramuscular or intravenous injection and to processes for manufacturing the same.

In the treatment of chronic diseases such as diabetes it is usual to give the patients three injections per day. As the injections are more or less painful it is obvious that in the long run this treatment will be very disagreeable for the patient. It has been tried to reduce the number of injections by incorporating in the solutions used substances which prolong the action of the insulin, a substance suggested for this purpose is the protamine obtained from salmon sperm (U. S. A. specification No. 2,076,082). As a matter of fact insulin solutions containing an addition of the protamine from salmon sperm show a prolonged action when compared with the insulin solutions without the said addition. However, insulin solutions containing protamine have considerable drawbacks. In the first place the mixture is not stable and must be agitated before being used; it contains the insulin in precipitated condition, and the mixture must be freshly prepared at frequent intervals. It is also undesirable to introduce more or less regularly foreign protein substances in the human system. Moreover the expenses of the addition of protamine are rather high.

I have now found that very favourable results can be obtained when pectin is incorporated in the insulin solutions. The presence of pectin in the solution to be injected has the unexpected result that the period of action of the insulin is substantially increased when compared with solutions which do not contain pectin. If the percentage of sugar in the blood after the insulin injection is determined at the end of different intervals it appears in the case of insulin solutions containing pectin that the period which the blood sugar content requires to reach its original value after the decrease due to the insulin is substantially longer than when the ordinary insulin solutions without pectin are used.

The favourable effect of pectin on the action of insulin solutions is shown by the drawing which illustrates the effect of the addition of pectin in a series of tests with rabbits. The ordinates represent the percentage of sugar in the blood in milligrams per 100 cm.³, the abscissae the time after injection of the insulin solution. As soon as the insulin has been injected a rapid decrease of the percentage of blood sugar will occur. After some time the blood sugar content

will increase again and after a few hours it will attain its original value. The variations of the blood sugar content in the test period are indicated by the curves 1-3.

Curve 1 shows the effect of an ordinary insulin solution containing insulin and hydrochloric acid, the hydrochloric acid concentration being 0.01 N.

Curve 2 gives the result of a test with a similar insulin solution containing 2½% of pectin.

Curve 3 relates to a test with a pectin solution containing 3½% of pectin.

The drawing clearly shows that in the last two cases the period of action of the insulin is substantially longer than in the first case where a solution without pectin is used.

The effect of the addition of pectin varies with the proportion of pectin used. It further depends to a certain extent on the hydrogen ion concentration of the solution used. Very favourable results are generally obtained with solutions which have a slight acid reaction, i. e. a pH slightly below the isoelectric point (5.0-5.4). A higher pH value will obviously be unsuitable since it will be outside the range of pH values in which the insulin is in dissolved condition. Solutions of this character are obtained by partly neutralizing the usual insulin solutions, which generally have a pronounced acid reaction, e. g. by adding the required amount of soda.

The use of insulin solutions according to the invention has considerable advantages. Owing to the longer period of action of the said solution the interval between the subsequent injections can be prolonged so that instead of the usual number of three injections per day two or even one injection will be satisfactory. Obviously it is of great value for a diabetes patient to have the number of injections substantially reduced. A further important advantage of the use of insulin solutions containing pectin is to be seen in the fact, that the amount of insulin given per day can be materially reduced.

I claim:

1. A substantially stable insulin solution suitable for hypodermic injection and having a prolonged insulin effect, said solution containing an amount of pectin ranging from about 2½ percent to about 3½ percent of the total amount of the solution.

2. A substantially stable insulin solution as defined in claim 1 said solution having a slightly acid reaction.

3. A substantially stable insulin solution suitable for hypodermic injection and having a pro-

longed insulin effect, said solution containing at least about 2½ percent of pectin calculated on the total amount of the solution.

4. A substantially stable insulin solution as defined in claim 3, said solution having a slightly acid reaction.

5. A substantially stable insulin solution suitable for hypodermic injection and having a pro-

longed insulin effect, said solution containing a small amount of pectin sufficient materially to prolong its insulin effect.

6. A substantially stable insulin solution as defined in claim 5, which has a slightly acid reaction.

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