

NPH insulin

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NPH insulin (or neutral protamine Hagedorn) (also known as Humulin N, Novolin N, Novolin NPH, NPH Iletin II, and isophane insulin), is an intermediate-acting insulin given to help control the blood sugar level of those with diabetes. NPH was created in 1936 when Nordisk formulated "isophane" porcine insulin by adding neutral protamine to regular insulin.

This is a suspension of crystalline zinc insulin combined with the positively charged polypeptide, protamine. When injected subcutaneously, it has an intermediate duration of action, meaning longer than that of regular insulin, and shorter than ultralente, glargine or detemir.

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History

Hans Christian Hagedorn (1888–1971) and August Krogh (1874–1949) obtained the rights for insulin from Banting and Best in Toronto, Canada. In 1923 they formed Nordisk Insulinlaboratorium, and in 1926 with August Kongsted he obtained a Danish Royal Charter as a non-profit foundation.

In 1936, Hagedorn and B. Norman Jensen discovered that the effects of injected insulin could be prolonged by the addition of protamine obtained from the "milt" or semen of river trout. The insulin would be added to the protamine, but the solution would have to be brought to pH 7 for injection. Canada later produced bok insulin, a mixture of zinc, protamine and porcine insulin. This mixture only needed to be shaken before injection.

In 1946, Nordisk was able to form crystals of protamine and insulin and marketed it in 1950 as NPH insulin. NPH insulin has the advantage that it can be mixed with an insulin that has a faster onset to complement its longer lasting action, which is the primary reason NPH remains on the market today, because manufacturers sell a variety of premixed insulin formulations. However, numerous medical studies have suggested that NPH has one of the least consistent absorption rates when injected subcutaneously, and a majority of head-to-head comparisons with Lente insulin usually found Lente provided superior glycemic control.

Eventually all animal insulins made by Novo Nordisk were replaced by synthetic, recombinant 'human' insulin. Synthetic 'human' insulin is also complexed with protamine to form NPH.

NPH insulin is cloudy and has an onset of 1–4 hours. Its peak is 6–10 hours and its duration is about 10–16 hours.

Administration

NPH insulin may be combined with faster acting insulin to allow more accurate dosing and better blood sugar level control. When administered this way, the two insulin types will normally be combined in the same syringe. NPH and fast-acting insulin bind when mixed, so they should not be combined until it is time to inject. Patients are instructed on the proper procedure to prepare this type of injection to minimize the likelihood of combining two types of insulin in the same vial. The proper order for withdrawing NPH insulin and fast-acting insulin into the same syringe can be remembered by the mnemonic "clear before cloudy", or fast acting clear insulin first, followed by NPH (cloudy). Aspiration, or pulling back on the plunger of the syringe after the needle has been injected to check for blood, is not appropriate for subcutaneous injections.

Timeline

- 1926 Nordisk receives Danish charter to produce insulin
- 1936 Hagedorn discovers that adding protamine to insulin prolongs the effect of insulin
- 1936 Canadians D.M. Scott and A.M. Fisher formulate zinc insulin mixture and license to Novo
- 1946 Nordisk crystallizes a protamine and insulin mixture
- 1950 Nordisk markets NPH insulin
- 1953 Nordisk markets "Lente" zinc insulin mixtures.

See also

- Insulin analogue

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