Typically, fast-acting insulins are administered to such subjects in response to hyperglycemia or in anticipation of hyperglycemia, such as following consumption of a meal, which can result in glycemic control. However, current fast-acting forms of insulins have a delay in absorption and action, and therefore do not approximate the rapid endogenous insulin action. Thus, such formulations do not act quickly enough to shut off hepatic glucose production that occurs shortly after this first phase of insulin release. Due to the delay in pharmacological action, the fast-acting insulin preparations should be administered in advance of meals in order to achieve the desired glycemic control. Further, the doses that must be administered lead to an extended duration of action that contributes to hypoglycemia, and in many cases, obesity. Hence, there is a need for alternative insulin compositions that more effectively mimic the endogenous insulin response when administered to a subject, leading to more effective glycemic control and a reduction in the negative side-effects of insulin therapy, such as weight gain.

SUMMARY

In a first aspect, there is provided a super fast-acting insulin composition, comprising:

a fast-acting insulin analog at a concentration of from about 10 U/mL to at or about 500 U/ml, wherein the fast-acting insulin analog is glulisine or insulin aspart; and

of a hyaluronidase at a concentration of 1 U/ml to 5000 U/ml, ; wherein:

a super fast-acting insulin composition is an insulin composition that has an onset of action that is faster than the analog alone, and a duration of action that is shorter than the analog alone, whereby, upon administration, the composition mimics the endogenous post-prandial insulin release of a nondiabetic subject; and

the super fast-acting insulin composition is formulated for a route of administration selected from among subcutaneous, intradermal and intraperitoneal administration.

In a second aspect, there is provided a syringe or vial, comprising the composition as defined above.

In a third aspect, there is provided a closed loop system, comprising the composition as defined above.

In a fourth aspect, there is provided an insulin pump, comprising the composition as defined above.

In a fifth aspect, there is provided an insulin pen, comprising the composition as defined above.

In a sixth aspect, there is provided an insulin pump for delivering super fast-acting insulin, comprising:

a fast-acting insulin analog, wherein the analog is insulin glulisine or insulin aspart at a concentration of 10 U/mL to 500 U/ml; and

a hyaluronidase at a concentration of 1-5000 U/ml, wherein:

the fast-acting insulin analog and the hyaluronidase are in the same or different reservoirs; and

the fast-acting insulin analog and the hyaluronidase , when combined, form a super fast-acting insulin, which has an onset of action that is faster than the analog alone, and a duration of action that is shorter than the analog alone, whereby, upon administration, the insulin closely mimics the physiologic post-prandial insulin response of a non-diabetic subject to achieve glycemic control.

In a seventh aspect, there is provided a method for making a super fast-acting insulin composition as defined above, comprising:

selecting insulin aspart or glulisine; and

combining it at a concentration of from about 10 U/mL to about 500 U/ml insulin with at least 1 U/ml of hyaluronidase.

In an eighth aspect, there is provided the use of a composition as defined above, for preparing a medicament for maintaining normal blood glucose levels in a subject.

In a ninth aspect, there is provided the use of a super fast-acting composition for preparing a medicament for administration to a diabetic less than 15 minutes before a meal up until 10 minutes after a meal or with a meal to control post-prandial blood glucose levels in the subject, wherein the composition, comprises:

a fast-acting insulin analog at a concentration of from 10 U/mL to a 500 U/ml; and

a hyaluronidase at a concentration of least 1U/ml, wherein

a super fast-acting insulin composition is an insulin composition that has an onset of action that is faster than the analog alone, and a duration of action that is shorter than the analog alone, whereby, upon administration, the composition mimics the endogenous post-prandial insulin release of a nondiabetic subject; and

the super fast-acting insulin composition is formulated for a route of administration selected from among subcutaneous, intradermal and intraperitoneal administration.

In a tenth aspect, there is provided a super fast-acting insulin composition for use for administration to a diabetic less than 15 minutes before a meal up until 10 minutes after a meal or with a meal to control post-prandial blood glucose levels in a subject, wherein the composition, comprises:

a fast-acting insulin analog at a concentration of from about 10 U/mL to at or about 500 U/ml; and

a hyaluronidase at a concentration of 1 U/ml to 5000 U/ml, wherein

a super fast-acting insulin composition is an insulin composition that has an onset of action that is faster than the analog alone, and a duration of action that is shorter than the analog alone, whereby, upon administration, the composition mimics the endogenous post-prandial insulin release of a nondiabetic subject; and

the super fast-acting insulin composition is formulated for a route of administration selected from among subcutaneous, intradermal and intraperitoneal administration.

Provided are super fast-acting insulin compositions that can act more rapidly and/or increase systemic exposure during a preselected time period compared to fast-acting compositions. Hence, provided are super fast-acting insulin compositions. The compositions contain a therapeutically effective amount of a fast-acting insulin and an amount of a hyaluronan degrading enzyme to render the composition super fast-acting. The compositions are formulated for parenteral administration, such as subcutaneous, intradermal or intramuscular administration. Insulin dosage (amount administered) can be determined by the quantity sufficient to achieve glycemic control, which can be determined empirically, such as by glucose challenge. Typically, a goal in treatment is to administer the lowest possible amount of insulin to achieve glycemic control and reduce the number of hyperglycemic and/or hypoglycemic events. The lower doses of insulin used in the super fast-acting insulin compositions can reduce the risk of weight gain and obesity in diabetic subjects. The compositions can be provided in any suitable container or vehicle, such as in a sterile vial, syringe, cartridge, insulin pen, insulin pump or in a closed loop system reservoir.