Treatment of Type I and Type II Diabetes

Field

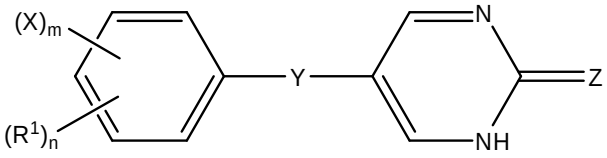
The present disclosure relates to methods of treating Type I or Type II diabetes in a mammal comprising administering insulin and a phenoxypyrimidinone compound, or pharmaceutically acceptable salts thereof, to the mammal, and to formulations thereto.

Background

Diabetes is the most common disorder of the endocrine system and occurs when blood sugar levels in the body consistently stay above normal. It affects more than 23 million people in the U.S. alone. Diabetes is a disease brought on by either the body's inability to make insulin (Type I diabetes) or by the body's inability to respond to the effects of insulin (Type II diabetes). It can also appear during pregnancy. Insulin is one of the main hormones that regulates blood sugar levels and allows the body to use sugar for energy. Once Type II diabetes develops, symptoms include unusual thirst, a frequent need to urinate, blurred vision, or extreme fatigue. Type I diabetes occurs because the insulin-producing cells of the pancreas, beta cells, are destroyed by the immune system. People with Type I diabetes produce no insulin and must use insulin injections to control their blood sugar. Type I diabetes most commonly starts in people under the age of 20, but may occur at any age. Thus, compounds and compositions that can be used to treat Type I and/or Type II diabetes are clearly needed.

Summary

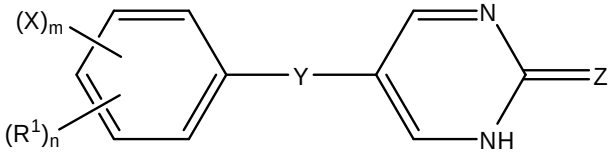
In one aspect, the present disclosure refers to use of a compound of Formula I:



I,

or a pharmaceutically acceptable salt thereof, wherein: R^1 is an alkyl group; X is a halogen; Y is O, S, or NH; Z is O or S; n is an integer from 0 to 5 and m is 0 or 1, wherein m + n is less than or equal to 5, in the manufacture of a medicament for the treatment of Type I diabetes in a mammal, wherein the treatment comprises insulin to be administered first followed by the compound or pharmaceutically acceptable salt thereof to be administered.

The present disclosure provides methods of treating Type I or Type II diabetes in a mammal comprising administering to the mammal in need thereof an effective amount of insulin and an effective amount of a compound of Formula I:

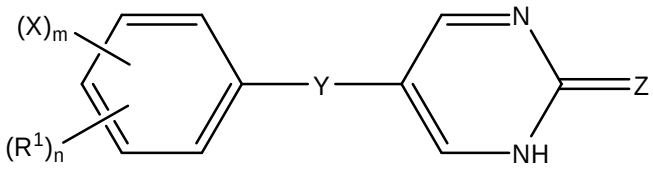


I,

or a pharmaceutically acceptable salt thereof, wherein: R^1 is an alkyl group; X is a halogen; Y is O, S, or NH; Z is O or S; n is an integer from 0 to 5 and m is 0 or 1, wherein m + n is less than or equal to 5.

What Is Claimed Is:

1. Use of a compound of Formula I:



I,

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is an alkyl group;

X is a halogen;

Y is O, S, or NH;

Z is O or S;

n is an integer from 0 to 5 and m is 0 or 1, wherein m + n is less than or equal to 5, in the manufacture of a medicament for the treatment of Type I diabetes in a mammal, wherein the treatment comprises insulin to be administered first followed by the compound or pharmaceutically acceptable salt thereof to be administered.

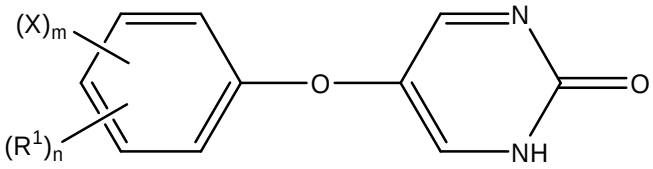
2. The use according to claim 1 wherein the alkyl group is methyl and n is 1.

3. The use according to claim 1 or claim 2, wherein the halogen is chlorine and m is 1.

4. The use according to any one of claims 1 to 3, wherein Y is O.

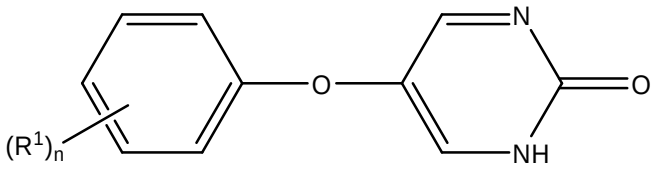
5. The use according to any one of claims 1 to 4, wherein Z is O.

6. The use according to any one of claims 1 to 5, wherein the compound is of Formula II:



II.

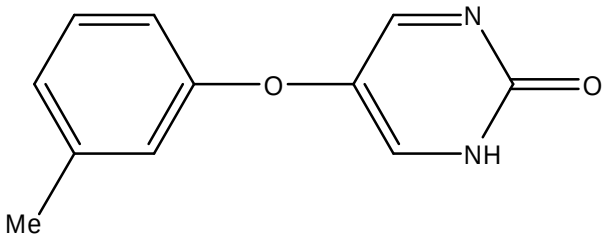
7. The use according to claim 1, wherein the compound is of Formula III:



III.

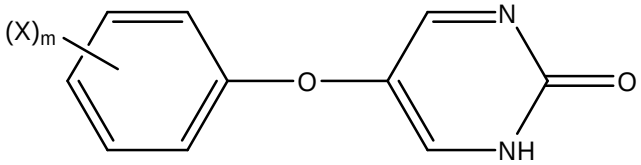
8. The use according to claim 7, wherein R^1 is methyl and n is 1.

9. The use according to claim 8, wherein R^1 is in the meta position and the compound is of the formula:



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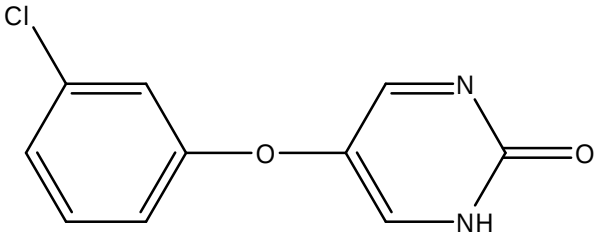
10. The use according to claim 1, wherein the compound is of Formula IV:



IV.

11. The use according to claim 10, wherein X is chlorine and m is 1.

12. The use according to claim 11, wherein X is in the meta position and the compound is of Formula VI:



VI.

13. The use according to any one of claims 1 to 12, wherein the mammal is a human.

14. The use according to any one of claims 1 to 13, wherein the amount of the compound is from about 0.1 mg/kg to about 100 mg/kg.

15. The use according to any one of claims 1 to 14, wherein the insulin is selected from: injectable insulin, transdermal insulin, and inhaled insulin.

16. The use according to any one of claims 1 to 14, wherein the insulin is selected from: rapid-acting insulin, short-acting insulin, intermediate acting insulin, and long-acting insulin.

17. The use according to claim 16, wherein the rapid acting insulin or short-acting insulin is: from about 0.05 U/kg/day to about 5 U/kg/day; from about 0.1 U/kg/day to about 2.5 U/kg/day; or from about 0.3 U/kg/day to about 0.8 U/kg/day.

18. The use according to claim 16, wherein the intermediate acting insulin or long-acting insulin is: from about 0.01 U/kg/day to about 3 U/kg/day; from about 0.05 U/kg/day to about 0.6 U/kg/day; or from about 0.1 U/kg/day to about 0.3 U/kg/day.

19. The use according to any one of claims 1 to 12, wherein the compound or pharmaceutically acceptable salt thereof is to be administered to the mammal 30 minutes after insulin had been administered.