

We claim:

1. A method of inhibiting Botulinum neurotoxin A metalloprotease activity which comprises contacting a compound selected from the group consisting of

Michellamine B;

NSC 357756;

NSC 119889

NSC 86372;

NSC 130796;

NSC 402959;

Q1-3;

Q1-19;

Q1-21;

Q2-11;

Q2-15;

Q2-43;

Q2-59;

Q2-61;

Q2-97;

Q3-53;

Q3-81; and

Q3-87

with a Botulinum neurotoxin A metalloprotease to inhibit the Botulinum neurotoxin A metalloprotease.

2. The method of claim 1, wherein the compound is in a composition.

3. The method of claim 2, wherein the composition further comprises a pharmaceutically acceptable carrier.

4. The method of claim 2, wherein the composition further comprises at least one supplementary active compound.

5. A method of inhibiting Botulinum neurotoxin A metalloprotease activity which comprises

screening a plurality of existing small molecule compounds for a small molecule compound that inhibits Botulinum neurotoxin A metalloprotease activity; and has a first plane A, a second plane B, a first hydrophobic moiety C, a second hydrophobic moiety D and a positive ionizable substituent E, wherein one or both of the planes comprise a biaryl group or a triaryl group and

(a) the distance between the center of the first plane A and the center of the second plane B is about 6.5 to about 9.5 Å;

(b) the distance between the center of the first hydrophobic moiety C and the center of the second hydrophobic moiety D is about 8.0 to about 16.0 Å;

(c) the distance between the center of the first plane to the center of the first hydrophobic moiety C is about 3.0 to about 5.0 Å;

(d) the distance between the center of the second plane to the center of the second hydrophobic moiety C is about 3.0 to about 5.0 Å; and

(e) the distance between the center of the first plane to the center of the positive ionizable substituent is about 6.5 to about 9.5 Å; and

contacting the small molecule compound with a Botulinum neurotoxin A metalloprotease to inhibit the Botulinum neurotoxin A metalloprotease.

6. The method of claim 5, wherein the small molecule compound further comprises a heteroatom in the first plane A.

7. The method of claim 5, wherein the biaryl group is selected from the group consisting of naphthalene, quinoline, isoquinoline, benzofuran, indole, quinazoline, quinoxaline, naphthyridine, phthalazine, and purine.

8. The method of claim 5, wherein the triacyl group is selected from the group consisting of acridine, phenazine, phenanthroline, phenanthridine, and carbazole.

9. The method of claim 5, wherein the hydrophobic moieties are capable of occupying the binding subsites 1 and 2 of the BoNT/A LC substrate binding cleft.

10. The method of claim 5, wherein the hydrophobic moieties are each independently selected from the group consisting of an alkyl group, bromo, chloro, iodo, alkoxy, and an unsaturated heterocycle.

11. The method of claim 5, wherein the positive ionizable substituent is selected from the group consisting of a primary amine, a secondary amine, or a tertiary amine moiety attached to an aromatic ring.

12. The method of claim 5, wherein the compound is a bisquinoline.

13. The method of claim 5, wherein the compound is selected from the group consisting of

Michellamine B;

NSC 357756;

NSC 119889

NSC 86372;

NSC 130796;

NSC 402959;

Q1-3;

Q1-19;

Q1-21;

Q2-11;

Q2-15;

Q2-43;

Q2-59;

Q2-61;

Q2-97;

Q3-53;

Q3-81; and

Q3-87.

14. The method of claim 5, wherein the compound is in a composition.

15. The method of claim 14, wherein the composition further comprises a pharmaceutically acceptable carrier.

16. The method of claim 14, wherein the composition further comprises at least one supplementary active compound.

17. A method of inhibiting Botulinum neurotoxin A metalloprotease activity which comprises

screening a plurality of existing small molecule compounds for a small molecule compound that inhibits Botulinum neurotoxin A metalloprotease activity and has a first plane A, a second plane B, a first hydrophobic moiety C, a second hydrophobic moiety D and a positive ionizable substituent E, wherein one or both of the planes comprise a biaryl group or a triaryl group and

(a) the distance between the center of the first plane A and the center of the second plane B is about 6.5 to about 9.5 Å;

(b) the distance between the center of the first hydrophobic moiety C and the center of the second hydrophobic moiety D is about 8.0 to about 16.0 Å;

(c) the distance between the center of the first plane to the center of the first hydrophobic moiety C is about 3.0 to about 5.0 Å;

(d) the distance between the center of the second plane to the center of the second hydrophobic moiety C is about 3.0 to about 5.0 Å; and

(e) the distance between the center of the first plane to the center of the positive ionizable substituent is about 6.5 to about 9.5 Å; and

contacting the small molecule compound with a Botulinum neurotoxin A metalloprotease to inhibit the Botulinum neurotoxin A metalloprotease,