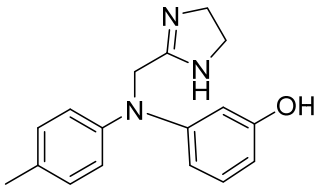
What is Claimed is:

1. A method for making phentolamine mesylate, comprising:

(a) allowing Compound **1**



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to react with methanesulfonic acid in the presence of acetone and water under conditions effective to make a first mixture comprising phentolamine mesylate;

(b) admixing the first mixture and methyl *t*-butyl ether to make a second mixture; and

(c) allowing the phentolamine mesylate to precipitate from the second mixture.

2. The method of claim 1, wherein allowing the phentolamine mesylate to precipitate from the second mixture comprises cooling the second mixture to a temperature of 15 ℃ to -25 ℃.

3. The method of claim 1 or 2, further comprising the step of:

(d) isolating the phentolamine mesylate from the second mixture, wherein the isolating provides isolated phentolamine mesylate.

4. The method of claim 3, wherein the isolating is filtering, and the isolated phentolamine mesylate is filtered phentolamine mesylate.

5. The method of claim 3, further comprising the step of:

(e) drying the isolated phentolamine mesylate to provide dried phentolamine mesylate.

6. The method of any one of claims 1-5, wherein the acetone and water are present in the first mixture of step (a) in a ratio of 10 (plus or minus up to 20%):1 acetone:water by volume to 12 (plus or minus up to 20%):1 acetone:water by volume.

7. The method of any one of claims 1-6, wherein Compound **1** is present in the first mixture of step (a) at a concentration of 0.2 (plus or minus up to 20%) moles/liter of the acetone and water to 0.4 (plus or minus up to 20%) moles/liter of the acetone and water.

8. The method of any one of claims 5-7, wherein the dried phentolamine mesylate has purity of at least 98% by weight of the dried phentolamine mesylate.

9. The method of any one of claims 5-7, wherein the dried phentolamine mesylate has a purity of 99.0% to 100% by weight of the dried phentolamine mesylate.

10. The method of any one of claims 5-9, wherein the dried phentolamine mesylate comprises less than 0.5% of an impurity by weight of the dried phentolamine mesylate.

11. The method of any one of claims 5-10, wherein the dried phentolamine mesylate is not subject to further purification.

12. Phentolamine mesylate that exhibits an X-ray powder diffraction (XRPD) pattern comprising a peak at 6.87 ± 0.2 degrees 2-theta, a peak at 11.65 ± 0.2 degrees 2-theta, a peak at 13.15 ± 0.2 degrees 2-theta, a peak at 18.86 ± 0.2 degrees 2-theta, a peak at 20.32 ± 0.2 degrees 2-theta, a peak at 20.85 ± 0.2 degrees 2-theta, a peak at 21.07 ± 0.2 degrees 2-theta, and a peak at 21.36 ± 0.2 degrees 2-theta.

13. The phentolamine mesylate of claim 12, wherein the phentolamine mesylate comprises less than 1% of an impurity by weight of the phentolamine mesylate.

14. The phentolamine mesylate of claim 13, comprising 0% water by weight to 8% water by weight of the phentolamine mesylate as determined by Karl Fischer titration.

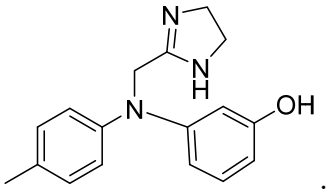
15. The phentolamine mesylate of claim 14, wherein the phentolamine mesylate comprises 0% water by weight to 6% water by weight of the phentolamine mesylate.

16. The phentolamine mesylate of claim 15, wherein the phentolamine mesylate comprises 0% water by weight to 3% water by weight of the phentolamine mesylate.

17. The phentolamine mesylate of any one of claims 14-16, wherein the phentolamine mesylate comprises less than 0.3% of the other impurity by weight of the phentolamine mesylate.

18. The phentolamine mesylate of any one of claims 14-16, wherein the phentolamine mesylate comprises less than 0.1% of the other impurity by weight of the phentolamine mesylate.

19. The phentolamine mesylate of any one of claims 14-18, wherein the other impurity is Compound **1** having the structure



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20. The phentolamine mesylate of any one of claims 14-18, wherein the other impurity is an alkyl methanesulfonate.

21. The phentolamine mesylate of any one of claims 14-18, wherein the other impurity is N-(2-aminoethyl)-2-[(3-hydroxyphenyl)(4-methylphenyl)amino]-acetamide, 2-chloromethyl-4,5-dihydro-1H-imidazole, or 3-hydroxy-4'-methyldiphenylamine, or a salt thereof.

22. A composition comprising the phentolamine mesylate of any one of claims 12-21 and a pharmaceutically acceptable carrier or excipient.

23. An ophthalmic solution comprising the phentolamine mesylate of claim 12 or 13.

24. The ophthalmic solution of claim 23, wherein the ophthalmic solution comprises the phentolamine mesylate in an amount of about 0.5% to about 2% by weight of the ophthalmic solution, wherein about is up to plus or minus 10%.

25. The ophthalmic solution of claim 23, wherein the ophthalmic solution comprises the phentolamine mesylate in an amount of about 1% by weight or volume of the ophthalmic solution, wherein about is up to plus or minus 10%.

26. Use of the phentolamine mesylate of any one of claims 12-21, the composition of claim 22, or the ophthalmic solution of any one of claims 23-25 in the manufacture of a medicament for inhibiting contraction of smooth muscle of a subject's iris.

27. Use of the phentolamine mesylate of any one of claims 12-21, the composition of claim 22, or the ophthalmic solution of any one of claims 23-25 in the manufacture of a medicament for reducing a subject's pupil diameter.

28. Use of the phentolamine mesylate of any one of claims 12-21, the composition of claim 22, or the ophthalmic solution of any one of claims 23-25 in the manufacture of a medicament for improving visual contrast sensitivity or visual acuity.

29. Use of the phentolamine mesylate of any one of claims 12-21, the composition of claim 22, or the ophthalmic solution of any one of claims 23-25 in the manufacture of a medicament for treating a dim or night vision disturbance.

30. Use of the phentolamine mesylate of any one of claims 12-21, the composition of claim 22, or the ophthalmic solution of any one of claims 23-25 in the manufacture of a medicament for treating or reversing pharmacologically induced mydriasis.

31. Use of the phentolamine mesylate of any one of claims 12-21, the composition of claim 22, or the ophthalmic solution of any one of claims 23-25 in the manufacture of a medicament for treating presbyopia.

32. The phentolamine mesylate of any one of claims 12-21, the composition of claim 22, or the ophthalmic solution of any one of claims 23-25 for use as a medicament.