PHARMACEUTICAL COMPOSITIONS AND METHODS OF TREATMENT

FIELD

The present invention relates to pharmaceutical compositions that can be used for the treatment of obesity and related metabolic disorders and for treating addiction to psychoactive substances, in particular nicotine.

BACKGROUND

Obesity is now recognized as a chronic disease that requires treatment to reduce its associated health risks. The increase in obesity is of concern because of the health risks associated with obesity, including coronary heart disease, strokes, hypertension, type 2 diabetes mellitus, dyslipidemia, sleep apnea, osteoarthritis, gall bladder disease, depression, and certain forms of cancer (e.g., endometrial, breast, prostate, and colon). The negative health consequences of obesity make it the second leading cause of preventable death in the United States. See, McGinnis M, Foege W H., *"Actual Causes of Death in the United States,"* JAMA, 270, 2207 12 (1993).

It is believed that 5-10% reduction of body weight can substantially improve metabolic values, such as blood glucose, blood pressure, and lipid concentrations.

Currently available prescription drugs for managing obesity generally reduce weight by inducing satiety or decreasing dietary fat absorption. Satiety is achieved by increasing synaptic levels of norepinephrine, serotonin, or both. For example, stimulation of serotonin receptor subtypes 1B, 1D, and 2C and 1- and 2-adrenergic receptors decreases food intake by regulating satiety. See, Bray G A, *"The New Era of Drug Treatment. Pharmacologic Treatment of Obesity: Symposium Overview,"* Obes. Res., 3(suppl 4), (1995). Adrenergic agents (e.g., diethylpropion, benzphetamine, phendimetrazine, mazindol, and phentermine) act by modulating central norepinephrine and dopamine receptors through the promotion of catecholamine release. Older adrenergic weight-loss drugs (e.g., amphetamine, methamphetamine, and phenmetrazine), which strongly engage in dopamine pathways, are no longer recommended because of the risk of their abuse. Fenfluramine and dexfenfluramine, both serotonergic agents used to regulate appetite, are no longer available for use.

Chapter 8. *Antibodies to S-100 protein in anxiety-depressive disorders in experimental and clinical conditions. In "Animal models in biological psychiatry"*, Ed. Kalueff A.V. N-Y, "Nova Science Publishers, Inc.", 2006, pp. 137-152, all of which are incorporated herein by reference.

There is a continuing need for new drug products with desired therapeutic efficacy for treatment of excess body mass or obesity and substance addiction.

SUMMARY

In one aspect of the present disclosure, there is provided a pharmaceutical composition comprising a homeopathically potentized form of an antibody to human cannabinoid receptor.

In one ~~aspect~~embodiment, the ~~invention~~present disclosure provides a pharmaceutical composition comprising an activated-potentiated form of an antibody to human cannabinoid receptor. Preferably, the human cannabinoid receptor is cannabinoid receptor 1 (CB1). It is contemplated that the activated-potentiated form of an antibody of this ~~aspect~~embodiment of the ~~invention~~present disclosure is to the entire human cannabinoid receptor 1. Specific sequences provided in the detailed description of the ~~invention~~present disclosure are specifically contemplated. It is contemplated that the activated-potentiated form of an antibody is to a polypeptide fragment of the human cannabinoid receptor 1. Preferably, the activated-potentiated form of an antibody is in the form of a mixture of C12, C30, and C200 homeopathic dilutions. In the particularly preferred variant, the activated-potentiated form of an antibody is in the form of a mixture of C12, C30, and C200 homeopathic dilutions impregnated onto a solid carrier. It is contemplated that the activated-potentiated form of an antibody to a human cannabinoid-receptor is a monoclonal, polyclonal or natural antibody. Preferably, the activated-potentiated form of an antibody to a human cannabinoid receptor is a polyclonal antibody. The antibody to human cannabinoid receptor may be prepared by successive centesimal dilutions coupled with shaking of every dilution.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides a method of treating obesity and related metabolic disorders, said method comprising administering the pharmaceutical composition of any variant or embodiment of the pharmaceutical composition ~~aspect~~embodiment of the ~~invention~~present disclosure. The pharmaceutical composition may be administered to a patient as one or two unit dosage forms from once daily to four times daily. Twice daily administration is specifically contemplated.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides a method of nicotine addiction, said method comprising administering the pharmaceutical composition of any variant or embodiment of the pharmaceutical composition ~~aspect~~embodiment of the ~~invention~~present disclosure. The pharmaceutical composition may be

administered to a patient as one or two unit dosage forms from once daily to four times daily. Twice daily administration is specifically contemplated.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides a method of altering anthropometric parameters of a mammal expected to benefit from such alteration, said method comprising administering the pharmaceutical composition of any variant or embodiment of the pharmaceutical composition ~~aspect~~embodiment of the ~~invention~~present disclosure. In one embodiment, the anthropometric parameter is waist circumference. In one embodiment, the anthropometric parameter is waist-height ratio. In another embodiment, the anthropometric parameter is waist-to-hip ratio. Various variants are provided.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides method of reducing body mass of a mammal, said method comprising administering the pharmaceutical composition of any variant or embodiment of the pharmaceutical composition ~~aspect~~embodiment of the ~~invention~~present disclosure. In one variant, the body mass is reduced by at least 5%. In another variant, the body mass is reduced by at least 10%. body mass is reduced by at least 15%. In another variant, the body mass is reduced by less than 15%.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides a method of reducing body mass growth of a mammal, said method comprising administering the pharmaceutical composition of any variant or embodiment of the pharmaceutical composition ~~aspect~~embodiment of the ~~invention~~present disclosure. In one variant, the body mass growth is reduced by at least 10%. In another variant, the body mass growth is reduced by at least 30%.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides a method of facilitating a reduction of food consumption in a mammal expected to benefit from such reduction, said method comprising administering the pharmaceutical composition of any variant or embodiment of the pharmaceutical composition ~~aspect~~embodiment of the ~~invention~~present disclosure.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides a pharmaceutical composition comprising an activated-potentiated form of an antibody to human cannabinoid receptor and an activated-potentiated form of an antibody to S-100 protein. In one variant, the antibody to the S-100 protein is an antibody to the entire S-100 protein. Sequences for S-100 protein are provided in the specification. Preferably, the antibody to the S-100 protein is in the form of mixture of C12, C30, and C200 homeopathic dilutions impregnated onto the solid carrier. The pharmaceutical

composition of this ~~aspect~~embodiment of the ~~invention~~present disclosure may contain antibody to S-100 protein which is a monoclonal, polyclonal or natural antibody. Preferably, the antibody to the S-100 protein is a polyclonal antibody. The antibody to the S-100 protein may be prepared by successive centesimal dilutions coupled with shaking of every dilution.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides a method of treating a patient suffering from a psychoactive substance addiction, said method comprising administering the pharmaceutical composition comprising an activated-potentiated form of an antibody to human cannabinoid receptor and an activated-potentiated form of an antibody to S-100 protein. Preferably, the psychoactive substance is nicotine. Preferably. the administration of said combination leads to a statistically significant improvement in the ability to tolerate the quitting of smoking as measured by analysis of data of the MPSS test. Preferably, the administration of said combination leads to a statistically significant reduction of smoking of in patients with moderate nicotine addiction as measured by the Fagerström Test for Nicotine Dependence Test. Preferably, the administration of said combination leads to a statistically significant reduction of smoking of in patients with heavy nicotine addiction as measured by the Fagerström Test for Nicotine Dependence Test.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides a pharmaceutical composition for use in treating a patient suffering from a psychoactive substance addiction, said composition having been obtained by providing a) a potentiated solution of an antibody to human cannabinoid receptor, and b) a potentiated solution of an activated-potentiated form of an antibody to S-100 protein, each prepared by consecutive repeated dilution and multiple vertical shaking of each obtained solution in accordance with homeopathic technology, and then either combining the potentiated solutions by mixing them, or, alternatively, impregnating a carrier mass with said combined solution or with the solutions separately.

In another ~~aspect~~embodiment, the ~~invention~~present disclosure provides pharmaceutical composition for use in treating obesity and related metabolic disorders, said composition having been obtained by providing a potentiated solution of an antibody to human cannabinoid receptor, prepared by consecutive repeated dilution and multiple vertical shaking of each obtained solution in accordance with homeopathic technology, and then optionally impregnating a carrier mass with said solution.

What is claimed is:

1. A pharmaceutical composition comprising an activated-potentiated form of an antibody to human cannabinoid receptor.

2. The pharmaceutical composition of claim 1, wherein said human cannabinoid receptor is cannabinoid receptor 1 (CB1).

3. The pharmaceutical composition of claim 2, wherein said activated-potentiated form of an antibody is to the entire human cannabinoid receptor 1.

4. The pharmaceutical composition of claim 3, wherein said entire human cannabinoid receptor 1 consists of sequence provided in SEQ ID No: 1.

5. The pharmaceutical composition of claim 2, wherein said activated-potentiated form of an antibody is to a polypeptide fragment of the human cannabinoid receptor 1.

6. The pharmaceutical composition of claim 5, wherein said polypeptide fragment of the human cannabinoid receptor 1 is selected from the group consisting of sequences provided in SEQ ID Nos: 3-16.

7. The pharmaceutical composition of claim 1, wherein said activated-potentiated form of an antibody is in the form of a mixture of C12, C30, and C200 homeopathic dilutions.

8. The pharmaceutical composition of claim 1, wherein said activated-potentiated form of an antibody is in the form of a mixture of C12, C30, and C200 homeopathic dilutions impregnated onto a solid carrier.

9. The pharmaceutical composition of claim 1, wherein the activated-potentiated form of an antibody to a human cannabinoid-receptor is a monoclonal, polyclonal or natural antibody.

10. The pharmaceutical composition of claim 9, wherein said activated-potentiated form of an antibody to a human cannabinoid-receptor is a polyclonal antibody.

11. The pharmaceutical composition of claim 1, wherein the antibody to human cannabinoid receptor is prepared by successive centesimal dilutions coupled with shaking of every dilution.

12. A method of treating obesity and related metabolic disorders, said method comprising administering the pharmaceutical composition of claims 1 or 2.

13. The method of claim 12, wherein said pharmaceutical composition is administered to a patient as one or two unit dosage forms from once daily to four times daily.

14. The method of claim 13, wherein said dosage form(s) is administered twice daily.

15. A method of altering anthropometric parameters of a mammal expected to benefit from such alteration, said method comprising administering the pharmaceutical composition of claims 1 or 2.

16. The method of claim 15, wherein said anthropometric parameter is waist circumference.

17. The method of claim 15, wherein said anthropometric parameter is waist-height ratio.

18. The method of claim 15, wherein said anthropometric parameter is waist-to-hip ratio.

19. The method of claim 16, wherein the waist circumference is reduced by at least 1%.

20. The method of claim 16, wherein the waist circumference is reduced by at least 2%.

21. The method of claim 16, wherein the waist circumference is reduced by at least 3%.

22. The method of claim 16, wherein the waist circumference is reduced by at least 1cm.

23. The method of claim 16, wherein the waist circumference is reduced by at least 3cm.

24. A method of reducing body mass of a mammal, said method comprising administering the pharmaceutical composition of claims 1 or 2.

25. The method of claim 24, wherein body mass is reduced by at least 5%.

26. The method of claim 24, wherein body mass is reduced by at least 10%.

27. The method of claim 24, wherein body mass is reduced by at least 15%.

28. The method of claim 24, wherein body mass is reduced by less than 15%.

29. A method of reducing body mass growth of a mammal, said method comprising administering the pharmaceutical composition of claims 1 or 2.

30. The method of claim 29, wherein body mass growth is reduced by at least 10%.

31. The method of claim 29, wherein body mass growth is reduced by at least 30%.

32. A method of facilitating a reduction of food consumption in a mammal expected to benefit from such reduction, said method comprising administering the pharmaceutical composition of claims 1.

33. The pharmaceutical composition of claims 1 or 2, further comprising activated-potentiated form of an antibody to S-100 protein.

34. The pharmaceutical composition of claim 33, wherein the antibody to the S-100 protein is an antibody to the entire S-100 protein.

35. The pharmaceutical composition of claim 34, wherein said entire S-100 protein consists of sequence provided in SEQ ID No: 17.

36. The pharmaceutical composition of claim 33, wherein the antibody to the S-100 protein is in the form of mixture of C12, C30, and C200 homeopathic dilutions impregnated onto the solid carrier.

37. The pharmaceutical composition of claim 33, wherein the antibody to the S-100 protein is a monoclonal, polyclonal or natural antibody.

38. The pharmaceutical composition of claim 37, wherein the antibody to the S-100 protein is a polyclonal antibody.

39. The pharmaceutical composition of claim 36, wherein the antibody to the S-100 protein is prepared by successive centesimal dilutions coupled with shaking of every dilution.

40. A method of treating a patient suffering from a psychoactive substance addiction, said method comprising administering the pharmaceutical composition of claim 33.

41. The method of claim 40, wherein said psychoactive substance is nicotine.

42. The method of claim 41, wherein said administration of said combination leads to a statistically significant improvement in the ability to tolerate the quitting of smoking as measured by analysis of data of the MPSS test.

43. The method of claim 41, wherein said administration of said combination leads to a statistically significant reduction of smoking of in patients with moderate nicotine addiction as measured by the Fagerström Test for Nicotine Dependence Test.

44. The method of claim 41, wherein said administration of said combination leads to a statistically significant reduction of smoking of in patients with heavy nicotine addiction as measured by the Fagerström Test for Nicotine Dependence Test.

45. A method of psychoactive substance addiction comprising administering the pharmaceutical composition of claim 33.

46. A pharmaceutical composition for use in treating a patient suffering from a psychoactive substance addiction, said composition having been obtained by providing a) a potentiated solution of an antibody to human cannabinoid receptor, and b) a potentiated solution of

an activated-potentiated form of an antibody to S-100 protein, each prepared by consecutive repeated dilution and multiple vertical shaking of each obtained solution in accordance with homeopathic technology, and then either combining the potentiated solutions by mixing them, or, alternatively, impregnating a carrier mass with said combined solution or with the solutions separately.

47. A pharmaceutical composition for use in treating obesity and related metabolic disorders, said composition having been obtained by providing a potentiated solution of an antibody to human cannabinoid receptor, prepared by consecutive repeated dilution and multiple vertical shaking of each obtained solution in accordance with homeopathic technology, and then optionally impregnating a carrier mass with said solution.

48. The method of claim 40, wherein said psychoactive substance addiction is nicotine.

What is claimed is:

1. A pharmaceutical composition comprising a homeopathically potentized form of an antibody to human cannabinoid receptor.

2. The pharmaceutical composition of claim 1, wherein said human cannabinoid receptor is cannabinoid receptor 1 (CB1).

3. The pharmaceutical composition of claim 2, wherein said homeopathically potentized form of an antibody is to the entire human cannabinoid receptor 1.

4. The pharmaceutical composition of claim 3, wherein said entire human cannabinoid receptor 1 consists of sequence provided in SEQ ID No: 1.

5. The pharmaceutical composition of claim 2, wherein said homeopathically potentized form of an antibody is to a polypeptide fragment of the human cannabinoid receptor 1.

6. The pharmaceutical composition of claim 5, wherein said polypeptide fragment of the human cannabinoid receptor 1 is selected from the group consisting of sequences provided in SEQ ID Nos: 3-16.

7. The pharmaceutical composition of claim 1, wherein said homeopathically potentized form of an antibody is in the form of a mixture of C12, C30, and C200 homeopathic dilutions.

8. The pharmaceutical composition of claim 1, wherein said homeopathically potentized form of an antibody is in the form of a mixture of C12, C30, and C200 homeopathic dilutions impregnated onto a solid carrier.

9. The pharmaceutical composition of claim 1, wherein the homeopathically potentized form of an antibody to a human cannabinoid-receptor is a monoclonal, polyclonal or natural antibody.

10. The pharmaceutical composition of claim 9, wherein said homeopathically potentized form of an antibody to a human cannabinoid-receptor is a polyclonal antibody.

11. The pharmaceutical composition of claim 1, wherein the antibody to human cannabinoid receptor is prepared by successive centesimal dilutions coupled with shaking of every dilution.