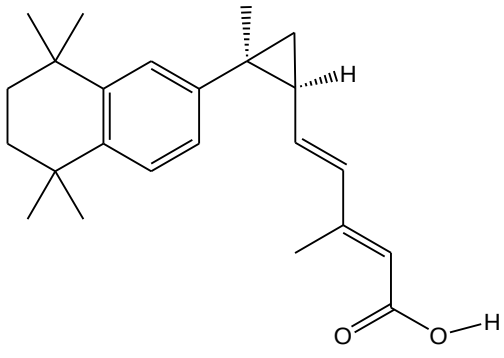
[0023a] Also disclosed herein is the use of a therapeutically effective amount of a RXR agonist and a thyroid hormone in the manufacture of a medicament for treating a nervous system disorder associated with neurodegeneration or demyelination, wherein the combination of the RXR agonist and the thyroid hormone is to be administered to an individual in need thereof, wherein administration of the combination of the RXR agonist and the thyroid hormone treats the nervous system disorder in the individual, wherein the selective RXR agonist is 3,7-dimethyl-6(S),7(S)-methano,7-[1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphth-7-yl]2(E),4(E) heptadienoic acid, and has the structure of formula III:



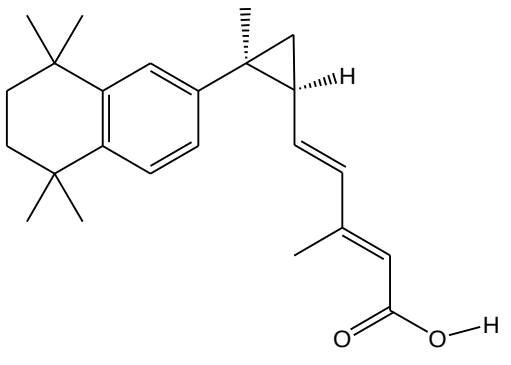
(III);

and wherein the combination of RXR agonist and thyroid hormone causes a greater improvement in the nervous system disorder than the selective RXR agonist or thyroid hormone alone.

BRIEF DESCRIPTION OF THE DRAWINGS

CLAIMS

1. Use of a therapeutically effective amount of a RXR agonist in the manufacture of a medicament for treating a nervous system disorder associated with neurodegeneration or demyelination, wherein the medicament is to be administered with a thyroid hormone to an individual in need thereof, wherein administration of the combination of the medicament and the thyroid hormone treats the nervous system disorder in the individual, wherein the selective RXR agonist is 3,7-dimethyl-6(S),7(S)-methano,7-[1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphth-7-yl]2(E),4(E) heptadienoic acid, and has the structure of formula III:



(III);

and wherein the combination of the medicament and thyroid hormone causes a greater improvement in the nervous system disorder than the medicament or thyroid hormone alone.

2. The use according to Claim 1 wherein the combination of the medicament and thyroid hormone treats the nervous system disorder in the individual by both promoting remyelination and neuroprotection of neurons and modulating the individual's immune system.

3. The use according to Claim 1, wherein the nervous system disorder is a central nervous system (CNS) disorder.

4. The use according to Claim 1, wherein the nervous system disorder is relapsing/remitting, primary progressive, and secondary progressive forms of multiple sclerosis (MS), diffuse white matter injury in pre-term infants, neuromyelitis optica, acute disseminated encephalomyelitis, Marburg multiple sclerosis, diffuse myelinoclastic sclerosis (Schilder's disease), Balo concentric sclerosis, solitary sclerosis, optic neuritis, transverse myelitis, amyotrophic lateral sclerosis (ALS), leukodystrophy (multiple variants, e.g. adrenoleukodystrophy, adrenomyeloneuropathy), Parkinson's disease, Alzheimer's disease, progressive supranuclear palsy, stroke, CNS trauma including traumatic brain injury and traumatic spinal cord injury, radiation induced neuroinflammation, radiation somnolence

syndrome, Devic's disease, inflammatory demyelinating diseases, CNS neuropathies, central pontine myelinolysis, Tabes dorsalis (syphilitic myelopathy), progressive multifocal leukoencephalopathy, leukodystrophy, depression, schizophrenia, epilepsy, or dementia.

5. The use according to claim 1, wherein the nervous system disorder is Parkinson’s Disease.

6. The use according to claim 1, wherein the nervous system disorder is Alzheimer’s Disease.

7. The use according to claim 1, wherein the nervous system disorder is a demyelination-related disorder.

8. The use according to Claim 7, wherein the demyelination-related disorder is multiple sclerosis.

9. The use according to Claim 7, wherein the demyelination-related disorder is radiation-induced central nervous system inflammation.

10. The use according to Claim 1, wherein the nervous system disorder is a peripheral nervous system disorder.

11. The use according to Claim 10, wherein the peripheral nervous system disorder is Guillain-Barré Syndrome, acute inflammatory demyelinating polyneuropathy, chronic inflammatory demyelinating polyneuropathy, demyelinating diabetic neuropathy, progressive inflammatory neuropathy, drug- or toxin-induced neuropathy, such as chemotherapy-induced neuropathy or organophosphate-induced neuropathy, anti-MAG peripheral neuropathy, Charcot-Marie-Tooth Disease, or copper deficiency.

12. The use according to Claim 1, wherein the therapeutically effective amount of the RXR agonist is:

1) 0.001 mg/day to 100 mg/day; or

2) 1 mg/day to 20 mg/day.

13. The use according to any one of Claims 1 to 12, wherein the thyroid hormone is thyroxine.

14. The use according to Claim 13, wherein the dose of thyroxine is 12.5 μg/day to 250 μg/day.

15. The use according to Claim 1, wherein the medicament is to be administered by nasal administration.

16. The use according to Claim 13, wherein both the medicament and thyroxine are to be administered by nasal administration.

17. The use according to Claim 1, wherein the medicament is to be administered orally.

18. The use according to Claim 13, wherein the medicament and the thyroxine are to be administered substantially simultaneously.

19. The use according to Claim 13, wherein the medicament and thyroxine are to be administered on different schedules.

20. The use according to Claim 1, wherein the thyroid hormone is to be administered orally or subcutaneously.

21. The use according to Claim 1, wherein treatment with the combination of the medicament and thyroid hormone reduces at least one symptom of the nervous system disorder, wherein the at least one symptom reduced is inflammation, fatigue, dizziness, malaise, elevated fever and high body temperature, extreme sensitivity to cold in the hands and feet, weakness and stiffness in muscles and joints, weight changes, digestive or gastrointestinal problems, low or high blood pressure, irritability, anxiety, or depression, blurred or double vision, ataxia, clonus, dysarthria, fatigue, clumsiness, hand paralysis, hemiparesis, genital anesthesia, incoordination, paresthesias, ocular paralysis, impaired muscle coordination, weakness (muscle), loss of sensation, impaired vision, neurological symptoms, unsteady gait, spastic paraparesis, incontinence, hearing problems, or speech problems.

22. The use according to Claim 1, further comprising:

determining free serum thyroxine; and

adjusting the dose of thyroid hormone to keep serum thyroxine levels in a euthyroid range.

23. The use of claim 1, wherein a neurotrophic factor, or neurotrophic factor mimetic is to be further administered.

24. The use of claim 23, wherein the neurotrophic factor is BDNF, GDNF, NGF, NT-3, bFGF, CNTF, NT-4/5, IGF, or insulin, or a mimetic thereof.

25. The use of claim 23, wherein the nervous system disorder is Parkinson’s disease, Alzheimer’s disease, a multiple sclerosis, an optic neuritis, a stroke, a nervous system trauma, amyotrophic lateral sclerosis, a neuropathy, a nervous system hypoxia, a nervous system toxicity, a dementia, a retinopathy, Huntington’s disease, a

synucleinopathy, epilepsy, autism, schizophrenia, depression, or and aging-related nervous system degeneration.

26. The use of claim 23, wherein:

1) the neurotrophic factor is GDNF, or a GDNF mimetic, and the nervous system disease is Parkinson's disease or amyotrophic lateral sclerosis;

2) the neurotrophic factor is BDNF and the nervous system disease is Alzheimer's disease, multiple sclerosis, stroke, nervous system trauma, aging, or dementia;

3) the neurotrophic factor is insulin or insulin-like growth factor, and the nervous system disease is Alzheimer's disease; or

4) the neurotrophic factor is BDNF, GDNF, or insulin, and the nervous system disease is aging-related CNS neurodegeneration.

27. The use of claim 23, wherein the neurotrophic factor or mimetic is to be administered by oral, parenteral, nasal, or topical routes, or by controlled release formulation with any of these routes of administration.

28. Use of a combination of a RXR agonist, a thyroid hormone, and a neurotrophic factor, or neurotrophic factor mimetic, for *in vitro* promotion of survival or growth of neurons or glial cells, for subsequent implantation into the nervous system of a patient with a nervous system disorder.