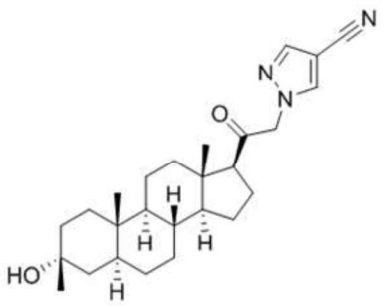
compositions that contain an isomerically pure form of the compound of Formula (I) preferentially target α4β3δ $GABA_A$ receptors, they are useful for therapeutic applications in which altering the activity of this receptor is beneficial.

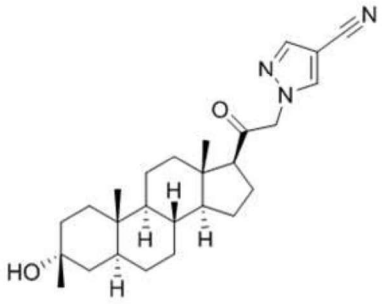
In an aspect, the present disclosure refers to a use of a pharmaceutical composition comprising an isomerically pure form of a compound of Formula (I):



(I),

in the preparation of a medicament for treatment of $GABA_A$ disorders, wherein the compound of Formula (I) is present in the medicament in a therapeutically effective amount to preferentially potentiate an α4β3δ $GABA_A$ receptor as compared to an α1β2γ2 $GABA_A$ receptor, wherein the $GABA_A$ disorder is selected from the group consisting of acute pain, an addictive disorder, Alzheimer's disease, Angelman's syndrome, anti-social personality disorder, an anxiety disorder, attention deficit hyperactivity disorder (ADHD), an attention disorder, an auditory disorder, autism, an autism spectrum disorder, bipolar disorder, chronic pain, a cognitive disorder, a compulsive disorder, a convulsive disorder, dementia, depression, dysthymia, an epileptic disorder, essential tremor, epileptogenesis, fragile X syndrome, generalized anxiety disorder (GAD), Huntington's disease, injury related pain syndrome, insomnia, ischemia, Lewis body type dementia, a memory disorder, migraines, a mood disorder, movement disorder, a neurodegenerative disease, neuropathic pain, an obsessive compulsive disorder, pain, a panic disorder, Parkinson's disease, a personality disorder, posttraumatic stress disorder (PTSD), psychosis, Rett syndrome, a schizoaffective disorder, schizophrenia, a schizophrenia spectrum disorder, a seizure disorder, a sleep disorder, social anxiety disorder, status epilepticus, stress, stroke, tinnitus, traumatic brain injury (TBI), vascular disease, vascular malformation, vascular type dementia movement disorder, Wilson's disease, and withdrawal syndrome.

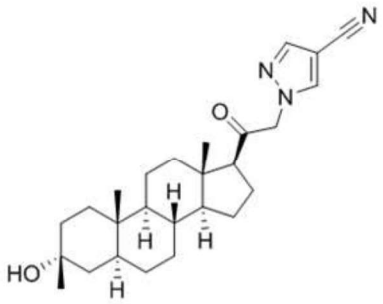
In an example, the disclosure provides pharmaceutical compositions containing an isomerically pure form of a compound of Formula (I):



(I),

wherein the compound of Formula (I) is present in a therapeutically effective amount to preferentially potentiate an α4β3δ $GABA_A$ receptor as compared to an α1β2γ2 $GABA_A$ receptor.

In another example, the disclosure provides methods for treating a $GABA_A$ disorder by providing to a subject a pharmaceutical composition comprising an isomerically pure form of a compound of Formula (I):



(I),

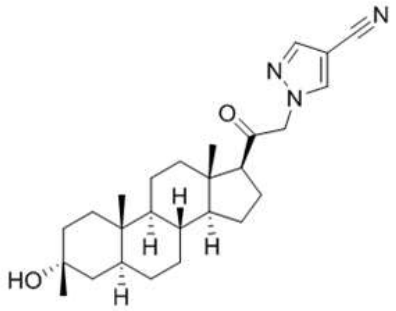
wherein the compound of Formula (I) is present in a therapeutically effective amount to preferentially potentiate an α4β3δ $GABA_A$ receptor as compared to an α1β2γ2 $GABA_A$ receptor.

The composition may be chemically pure, i.e., free from other molecules or chemical species. For example, the other molecule or chemical species may have a distinct chemical

Claims

What is claimed is:

1. Use of a pharmaceutical composition comprising an isomerically pure form of a compound of Formula (I):



(I),

in the preparation of a medicament for treatment of $GABA_A$ disorders, wherein the compound of Formula (I) is present in the medicament in a therapeutically effective amount to preferentially potentiate an $\alpha4\beta3\delta$ $GABA_A$ receptor as compared to an $\alpha1\beta2\gamma2$ $GABA_A$ receptor, wherein the $GABA_A$ disorder is selected from the group consisting of acute pain, an addictive disorder, Alzheimer's disease, Angelman's syndrome, anti-social personality disorder, an anxiety disorder, attention deficit hyperactivity disorder (ADHD), an attention disorder, an auditory disorder, autism, an autism spectrum disorder, bipolar disorder, chronic pain, a cognitive disorder, a compulsive disorder, a convulsive disorder, dementia, depression, dysthymia, an epileptic disorder, essential tremor, epileptogenesis, fragile X syndrome, generalized anxiety disorder (GAD), Huntington's disease, injury related pain syndrome, insomnia, ischemia, Lewis body type dementia, a memory disorder, migraines, a mood disorder, movement disorder, a neurodegenerative disease, neuropathic pain, an obsessive compulsive disorder, pain, a panic disorder, Parkinson's disease, a personality disorder, posttraumatic stress disorder (PTSD), psychosis, Rett syndrome, a schizoaffective disorder, schizophrenia, a schizophrenia spectrum disorder, a seizure disorder, a sleep disorder, social anxiety disorder, status epilepticus, stress, stroke, tinnitus,

traumatic brain injury (TBI), vascular disease, vascular malformation, vascular type dementia movement disorder, Wilson's disease, and withdrawal syndrome.

2. The use of claim 1, wherein the compound of Formula (I) preferentially positively modulates an α4β3δ $GABA_A$ receptor as compared to an α1β2γ2 $GABA_A$ receptor.

3. The use of claim 2, wherein an EC_{50} of the compound of Formula (I) for an α4β3δ $GABA_A$ receptor is less than 50% of an EC_{50} of the compound of Formula (I) for an α1β2γ2 $GABA_A$ receptor.

4. The use of claim 3, wherein an EC_{50} of the compound of Formula (I) for an α4β3δ $GABA_A$ receptor is less than 20% of an EC_{50} of the compound of Formula (I) for an α1β2γ2 $GABA_A$ receptor.

5. The use of claim 1, wherein an EC_{50} of the compound of Formula (I) for an α4β3δ $GABA_A$ receptor is less than 500 nM.

6. The use of any one of claims 1 to 5, wherein the $GABA_A$ disorder is an epileptic disorder, epileptogenesis, or a seizure disorder.

7. The use of claim 1, wherein the composition is formulated for oral administration.

8. The use of claim 1, the composition is formulated as a single daily dosage.