**Description**

**A COMPOSITION CONTAINING PYRANOSINE DERIVATIVES THAT EXHIBIT THE CHARACTERISTIC OF TRIGGERING AN INCREASE IN THE ACTIVITY OF AROMATIC AMINO ACID DECARBOXYLASE AND THE USE OF THIS COMPOSITION FOR THE TREATMENT OF DOPAMINERGIC DEFECTS**

**Technical Field**

The invention relates to a composition containing pyranosine derivatives formed for triggering an increase in the activity of aromatic amino acid decarboxylase.

**State of the Art**

Aromatic amino acid decarboxylase (AADC) is an enzyme that catalyzes the conversion of L-dopa to dopamine and the conversion of 5-hydroxytryptophan to serotonin. The patients with the deficiency of aromatic amino acid decarboxylase have the axial hypotonia, hypokinesia, athetosis, dystonia and rigidity in the extremities in the first months of their life. The seizure-mimicking oculogyric crises and convergent spasms are observed. The autonomic symptoms are also present, such as ptosis, nasal congestion, hypothermia, sweating, instability in the body temperature and fluctuations in the blood pressure. Sleep abnormalities, feeding difficulty and gastroesophageal reflux frequently accompany the clinical picture. These patients usually do not have seizure, and the oculogyric crises and autonomic nervous system symptoms are erroneously interpreted as seizure. In some patients with biochemical symptoms of AADC deficiency emerging with seizures during the neonatal period, PLP-responsive PNPO deficiency was detected afterwards. The clinical course is not very good in the case of AADC deficiency where there are serious problems in motor and language development.

In the case of deficiency, the dopamine and serotonin concentrations are lowered in BOS, as well as the concentrations of HVA and 5HIAA, which are the degradation products of the same. L-dopa is increased in BOS and the vanil lactic acid is excreted via urine. The diagnosis is made by way of metabolite analysis in BOS, measurement of enzyme activity in serum and the demonstration of mutation in the AADC gene. The patients with aromatic amino acid decarboxylase are treated with dopamine agonists, monoamine oxidase inhibitors and trihexyphenidyl.

According to the state of the art, the invention no. EP1337655B1 with classification "C12N 15/85" entitled "Lentiviral vectors for the treatment of neurodegenerative diseases" relates to retroviral vector genomes and to vector systems comprising such genomes. In particular the present invention relates to a retroviral vector genome comprising two or more NOIs operably linked by one or more Internal Ribosome Entry Site(s); a lentiviral vector genome comprising two or more NOIs suitable for treating a neurodegenerative disorder; and a lentiviral vector genome which encodes tyrosine hydroxylase, GTP-cyclohydrolase I and optionally Aromatic Amino Acid Dopa Decarboxylase.

Further, the invention no. EP1303278B1 entitled "Combination of a transdermal therapeutic system and an oral and/or parenteral preparation containing dopamine agonists for the treatment of dopaminergic disease states" relates to the use of a dopamine agonist in the form of an agent, comprising at least two physically separate compositions, of which one is a transdermal therapeutic system (TTS), containing the dopaminergic agent and one or several other compositions containing the same dopaminergic agent and suitable for oral and/or parenteral administration. Said compositions are suitable for the individually dosed and controlled treatment of dopaminergically treatable diseases with the following elements: a) the TTS is continuously applied, b) within the duration of application in a) the composition for oral or parenteral dosage is administered.

Further, the invention no. EP2074998B1 entitled "Use of cyclic bioisosteres of purine system derivatives for the treatment of diseases caused by disorders of nitrergic and dopaminergic system" relates to medicine, in particular, to pharmaceutical compositions having a directed action to important mediator systems of an organism, in particular, for the treatment of diseases associated with nitrergic and dopaminergic systems of an organism which are disorders caused by drug abuse selected from the group consisting of dependencies on narcotics, alcohol and nicotine.

As a result, the presence of the need for a composition for triggering an increase in the activity of aromatic amino acid decarboxylase and the inadequacy of the existing solutions have made it necessary to perform an improvement in the relevant art.

**Object of the Invention**

In order to eliminate the disadvantages of the state of the art, an object of the invention is to enable the stimulation of an increase in the activity of aromatic amino acid decarboxylase.

Another object of the invention is to enable the triggering of the regeneration by means of an increase in igf-1 in substantia nigra.

Another object of the invention is to enable an increase in the density of dopamine 1 receptor.

In order to achieve the aforesaid advantages, the invention is a composition for triggering an increase in the activity of aromatic amino acid decarboxylase, said composition being obtained by the components selected from the group comprising 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​1-​(hydroxyethyl)-​2-​(4-​aminophenyl)ethyl]-​pyranosine-taurinate, 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​4-​(dihydroxyethyl)-​2-​(4-​fluorophenyl)methyl]-​pyranosine that are used individually or in combinations.

The structural and characteristic features and all the advantages of the invention will become more clearly understood from the detailed description provided below and therefore, the evaluation must be made taking this detailed description into consideration.

**Detailed Description of the Invention**

The invention is a composition containing pyranosine derivatives formed for triggering an increase in the activity of aromatic amino acid decarboxylase. Said invention enables the stimulation of an increase in the activity of aromatic amino acid decarboxylase, enables the triggering of the regeneration by means of an increase in igf-1 in substantia nigra, and enables an increase in the density of dopamine 1 receptor.

The composition according to the invention contains 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​1-​(hydroxyethyl)-​2-​(4-​aminophenyl)ethyl]-​pyranosine-taurinate, 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​4-​(dihydroxyethyl)-​2-​(4-​fluorophenyl)methyl]-​pyranosine.

Said composition is obtained by a mixture of the aforesaid components according to the following ratios by weight:

1-99% 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​1-​(hydroxyethyl)-​2-​(4-​aminophenyl)ethyl]-​pyranosine-taurinate,

99-1% 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​4-​(dihydroxyethyl)-​2-​(4-​fluorophenyl)methyl]-​pyranosine.

The composition is obtained from the aforesaid components selected from the aforesaid group and used according to the mentioned weight ratio ranges individually or in combinations.

Said invention also encompasses the use of said composition for triggering an increase in the activity of aromatic amino acid decarboxylase and for treating the dopaminergic defects and the manufacture thereof for this purpose.

**CLAIMS**

1. A composition for triggering an increase in the activity of aromatic amino acid decarboxylase, said composition being obtained by the components selected from the group comprising 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​1-​(hydroxyethyl)-​2-​(4-​aminophenyl)ethyl]-​pyranosine-taurinate, 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​4-​(dihydroxyethyl)-​2-​(4-​fluorophenyl)methyl]-​pyranosine that are used individually or in combinations.
2. A composition according to Claim 1 characterized in that it comprises 1-99% by weight 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​1-​(hydroxyethyl)-​2-​(4-​aminophenyl)ethyl]-​pyranosine-taurinate.
3. A composition according to Claim 1 characterized in that it comprises 99-1% by weight 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​4-​(dihydroxyethyl)-​2-​(4-​fluorophenyl)methyl]-​pyranosine.
4. Use of the components according to Claims 1 to 3 obtained individually or in combinations selected from the group consisting of 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​1-​(hydroxyethyl)-​2-​(4-​aminophenyl)ethyl]-​pyranosine-taurinate, 2,​2-​difluoro-​N-​[(1R,​2R)-​2-​hydroxy-​4-​(dihydroxyethyl)-​2-​(4-​fluorophenyl)methyl]-​pyranosine for the manufacture of a composition for triggering an increase in the activity of aromatic amino acid decarboxylase and for treating dopaminergic defects.

**ABSTRACT**

**A COMPOSITION CONTAINING PYRANOSINE DERIVATIVES THAT EXHIBIT THE CHARACTERISTIC OF TRIGGERING AN INCREASE IN THE ACTIVITY OF AROMATIC AMINO ACID DECARBOXYLASE AND THE USE OF THIS COMPOSITION FOR THE TREATMENT OF DOPAMINERGIC DEFECTS**

The invention relates to a composition containing pyranosine derivatives formed for triggering an increase in the activity of aromatic amino acid decarboxylase and for treating dopaminergic defects.

No figure.