Abstract:
The invention relates to a composition for treating the neuroendocrinial damage caused by the autoimmune diseases.
A COMPOSITION FOR THE TREATMENT OF NEUROENDOCRINAL DAMAGE CAUSED BY AUTOIMMUNE DISEASES

Technical Field

The invention relates to a composition comprising dioscin derivatives and 98-E, eurycoma longifolia and cissus extracts for treating the neuroendocrinal damage caused by the autoimmune diseases.

State of the Art

Autoimmunity is the general name for the reactions that develop due to the hypersensitivity of the immune system. In the case of autoimmunity, the immune system mistakenly detects the body's own constituent tissues as "intruding matter", fails to recognize these tissues and produces antibodies against them; hence the immune system cells attack the body's own constituent tissues.

In addition, nearly all the autoimmune diseases, although not high in number, are of the idiopathic nature; in other words, their causes have not been fully understood.

The corticosteroids are employed in the treatment of the autoimmune diseases as a general rule.

Some of the autoimmune diseases widely known at the present may be listed as follows: Systemic lupus erythematosus (SLE), sarcoidosis, idiopathic pulmonary fibrosis, behcet's disease, canine myositis eosinophilica, hypogammaglobulinemia, meniere syndrome, juvenile rheumatoid arthritis, kawasaki disease, wilson syndrome, multiple sclerosis, ankylosing spondylitis.

Currently, the definitive treatment is not still possible for the autoimmune diseases. There is the hope that the definitive treatment may be obtained for the autoimmune diseases by the use of the stem cells. The studies are under way on the destruction of the T cells that detect the own cells of a body as the intruding matter and the transplantation of the blood stem cells producing the normal healthy T cells to
Another treatment method employed according to the state of the art involves the control and suppression of the genetic mechanism in the cells of the immune system. The cells of the immune system secrete various molecules when they are activated. The synthesis of these molecules is under the control of some genes. It is expected to alter the genetic structure in the stem cells to be able to take these genes under control. In this way, the secretion of the substances harming the body would be prevented. These genetically engineered stem cells, when administered back to the patient, produce normal T and B cells that do not harm the body's own cells.

The invention no. EP1933869B1 entitled "Use of IL-23 and IL-17 antagonists for treating the autoimmune inflammatory eye disease" deals with the novel methods and drug products involving the administration of the substances, which antagonize one or both of the activity of IL-23 and IL-17 in order to treat the autoimmune inflammatory eye disease.

Further, the invention no. EP1951687B1 entitled "N-Hydroxyamide derivatives and the use thereof relates to the N-hydroxyamide derivatives, their pharmaceutical composition, the methods for the preparation of the same and the use thereof for the treatment and/or prophylaxis of the autoimmune disorders and/or inflammatory diseases, cardiovascular diseases, neurodegenerative diseases, cancer, respiratory diseases and fibrosis. The invention relates specifically to N-hydroxyamide derivatives for the modulation, particularly the inhibition of the activity or function of the matrix metalloproteinases.

Further, the invention no. EP2056807B1 entitled "Treatment of the Inflammatory Diseases" relates generally to the inflammatory diseases of the peripheral nervous system. More particularly, the invention relates to the methods for treating the inflammatory diseases of the peripheral nervous system by way of the modulation of the sphingosine-1-phosphate receptor activity. In an embodiment, the invention provides a method consisting of the administration of an effective amount of FTY720
in order to treat a subject with chronic inflammatory demyelinating polyneuropathy (CIDP) disease or other autoimmune neuropathies.

As result, the presence of the need for a composition for treating the neuroendocrinal damage caused by the autoimmune diseases 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 treat the neuroendocrinal damage caused by the autoimmune diseases.

Another object of the invention is to increase the NGF expression, thereby supporting the production of new nerve cells.

Another object of the invention is to support the axone regeneration rate and the presynaptic neurotransmission.

Another object of the invention is to suppress IL-4, IL-6 and tnf-alpha.

Another object of the invention is to stimulate the repair of the muscle and connective tissue.

Another object of the invention is to promote the production of testosterone.

In order to achieve the aforesaid advantages, the invention is a composition for treating the neuroendocrinal damage caused by the autoimmune diseases, said composition being obtained by the components selected from the group comprising dimethyldioscin, 98-e, eurycoma longifolia extract, cissus extract that are used individually or in combinations.
therefore, the evaluation must be made taking this detailed description into consideration.

**Detailed Description of the Invention**

The invention is a composition comprising dioscin derivatives and 98-E, eurycoma longifolia and cissus extracts for treating the neuroendocrinal damage caused by the autoimmune diseases.

Dimethyl dioscin and 98-E, ingredients of the invention, increase the NGF expression, thereby supporting the production of new nerve cells. Dimethyldioscin and 98-E also support the axone regeneration rate and the presynaptic neurotransmission.

Eurycoma longifolia extract (100:1) and Cissus extract (5:1, 10:1), other ingredients of the invention, suppress immunoglobulin E, IL-4, IL-6 and tnf-alpha. Eurycoma longifolia extract (100:1) and Cissus extract also stimulate the repair of the muscle and connective tissue. Eurycoma longifolia extract (100:1) and Cissus extract also promote the production of testosterone.

The composition according to the invention contains dimethyldioscin, 98-e, eurycoma longifolia extract (100:1), cissus extract (5:1), (10:1).

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

- 13-28% dimethyldioscin,
- 17-44% 98-e,
- 50-18% eurycoma longifolia extract (100:1),
- 20-10% cissus extract (5:1), (10:1).

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 treating the neuroendocrinal damage caused by the autoimmune diseases and the manufacture thereof for this purpose.
1. A composition for treating the neuroendocrinal damage caused by the autoimmune diseases, said composition being obtained by the components selected from the group comprising dimethyldioscin, 98-e, eurycoma longifolia extract, cissus extract that are used individually or in combinations.

2. A composition according to Claim 1 characterized in that it comprises 13-28% by weight dimethyldioscin.

3. A composition according to Claim 1 characterized in that it comprises 17-44% by weight 98-e.

4. A composition according to Claim 1 characterized in that it comprises 50-18% by weight eurycoma longifolia extract (100:1).

5. A composition according to Claim 1 characterized in that it comprises 20-10% by weight cissus extract (5:1).

6. A composition according to Claim 1 characterized in that it comprises 20-10% by weight cissus extract (10:1).

7. Use of the components according to Claims 1 to 6 obtained individually or in combinations from the group consisting of dimethyldioscin, 98-e, eurycoma longifolia extract, cissus extract for the manufacture of a composition for treating the neuroendocrinal damage caused by the autoimmune diseases.
### A. CLASSIFICATION OF SUBJECT MATTER

- **INV.** A61K36/87  A61K36/185  A61P37/00

### ADD.

According to International Patent Classification (IPC) or to both national classification and IPC.

### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols):

- A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched.

Electronic database consulted during the international search (name of database and, where practicable, search terms used):

- EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>TR 2011 10106 A2 (ERDAL CAN ALKOCLAR [TR]) 21 September 2012 (2012-09-21) page 6, line 11 - page 7, line 29; claims</td>
<td>1,4,7</td>
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<td>X</td>
<td>WO 2010/140170 Al (SUNEV PHARMA SOLUTION LTD [IN]) 9 December 2010 (2010-12-09) pages 12-18; example 1-8 page 18, paragraph 2 page 4, line 3 page 7, paragraph 2 page 12; example 3, 4 claims 1, 4, 9</td>
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<td>WO 02/085394 Al (KHAMAR BAKULESH MAFATLAL [IN]; MOODY VANDANA DASHARATHBHAI [IN]; PANDYA) 31 October 2002 (2002-10-31) pages 12-18; example 1 page 18, paragraph 2 claims 1-4, 26-28</td>
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* Special categories of cited documents:

- **"A"** document defining the general state of the art which is not considered to be of particular relevance.
- **"E"** earlier application or patent but published on or after the international filing date.
- **"L"** document which may throw doubts on the priority claim(s) on which is cited to establish the publication date of another citation or other special reason (as specified).
- **"O"** document referring to oral disclosure, use, exhibition or other means.
- **"P"** document published prior to the international filing date but later than the priority date claimed.

- **"T"** later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention.
- **"X"** document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone.
- **"Y"** document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- **"A"** document member of the same patent family.

### Date of the actual completion of the international search

31 January 2014

### Date of mailing of the international search report

07/02/2014

### Name and mailing address of the ISA

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Form PCT/ISA/210 (second sheet) (April 2005)
INTERNATIONAL SEARCH REPORT

Box No. II  Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. No boxes filled. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. X claims Nos.: 2, 3 (completely); 1, 7 (partially) because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210

3. No boxes filled. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III  Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. No boxes filled. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. No boxes filled. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. No boxes filled. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No boxes filled. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

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Form PCT/ISA/21 0 (continuation of first sheet (2)) (April 2005)
Continuation of Box II.2

Claims Nos.: 2, 3 (completely); 1, 7 (partially)

Present claims 1-3 and 7 fail to meet the requirements of Articles 17(2) PCT to such an extent that no meaningful search can be made. The terms "dimethyl dioctyl" and "98-E" in claims 1-3 and 7 have no well recognized meaning (Article 6 PCT). Moreover, the meaning of these terms is not specified in the description and it is not possible to establish the chemical structure of the compounds.

In such a situation, the skilled person is not able to carry out the invention. The requirements of Article 5 PCT are not met.

Non-compliance with the substantive provisions is such that a meaningful search of the claimed subject-matter can not be carried out (Article 17(2) PCT).

Moreover, it is not possible to determine the subject matter that may be reasonably expected to be claimed.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on a matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter 11 procedure. If the applicant proceeds into the international phase before the EPO, the applicant is reminded that a search may be carried out during examination on before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.
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