Exhibit 26

Secretary's Advisory Committee on Genetics, Health, and Society

Public Consultation Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests

For Public Comment from March 9 to May 15, 2009

> It was only after considerable pressure from the scientific community that the company added methods to detect these deletions, insertions, and re-arrangements in 2006, over 10 years after they first introduced clinical genetic testing, and barred anyone else from performing the tests. In a competitive marketplace, this delay never would have occurred.[247]

Myriad disagrees with this characterization and notes that it launched testing for the five most common rearrangements, accounting for approximately one-third of all rearrangements, in 2002. Myriad also asserts that the rearrangement testing it was conducting at the time would have detected roughly one-third of the "missing" cases reported in the *JAMA* article. The company incorporated more extensive testing for rearrangements in 2006, the same year the *JAMA* article was published. The general trend for all diagnostic genetic testing has been to move toward more comprehensive analyses that detect deletions and rearrangements, and Myriad's actions have been consistent with the general trend. Indeed, in areas where there is no sole provider, there has been a similar lag in detecting deletions and rearrangements. Part of the delay in developing such analyses could reflect increased technical difficulty in testing for deletions and rearrangements.

Myriad's patent enforcement activities have been a source of the majority of the criticism against the company's *BRCA1* and *BRCA2* patents. A 2003 survey of laboratory directors found nine instances of enforcement of the *BRCA* patents by Myriad. This same group reported two instances of FAP patent enforcements and no cases of HNPCC patent enforcement.[248] Of 31 collected gene patent litigation cases, 5 of which were related to

[247] Dr. Chung's testimony appeared as an appendix to the written testimony of Dr. Marc Grodman presented to the House Judiciary Subcommittee on Courts, the Internet and Intellectual Property during a hearing held on October 30, 2007. Testimony is available at http://judiciary.house.gov/hearings/pdf/Grodman071030.pdf.

[248] Cho, M., et al. (2003). Effect of patents and licenses on the provision of clinical genetic testing services. *Journal of Molecular Diagnostics* 5(1):3-8. NB: FAP and HNPCC "patent enforcements" are more unlikely, given nonexclusive licensing and multiple rights holders.

How did patents and licensing practices affect price?

The case studies attempted to evaluate how patents and licensing practices affected the price of genetic tests, but could not always reach definite conclusions because of difficulties in obtaining relevant data and challenges in determining the relative contribution of various factors, including overhead costs, to price. For two of the case studies (Alzheimer's disease and LQTS), some findings suggest that the price of the patent-protected test was higher than it would have been had the test been unpatented, with the potential that this price is reducing patient utilization of the test. In addition, it appears that the test developers of the Canavan disease genetic test used their patent monopoly to establish restrictive license conditions and sought fees that exceeded what laboratories offering similar tests for Tay-Sachs disease were willing to pay. Angered by these terms, a consortium organized against the patent holder, initiated a lawsuit roughly a year after the license terms were first proposed, and negotiated a settlement that altered the license terms in a way that the plaintiffs apparently considered acceptable. One surprising finding from the case studies was that the per-unit price of the full-sequence *BRCA* test, which often is cited as being priced very high, was actually quite comparable to the price of other full-sequence tests done by polymerase chain reaction (PCR), at both nonprofit and for-profit testing laboratories.

Thus, there is at least the risk that a patent-protected genetic test will have an inflated price; this inflated price, in turn, may reduce how many patients use the test. Licensing many providers may mitigate price inflation. However, various factors other than patenting and licensing affect the price of genetic tests, including ordinary market forces, such as demand and market size (where there is a large market and high demand, the company stands to make considerable revenue even at a lower price). Many of these factors exert a downward pressure on price. For instance, health insurance providers often will not cover a test that is priced too high, so companies choose to keep the price low so that the test will be covered, which in turn makes the test more affordable to patients. Similarly, a company also has an incentive to set its price in the price range of other genetic tests covered by Medicare, Medicaid, and other private payers (by a formula for

Exhibit 27

US007341750B2

(12) **United States Patent**
Lee et al.

(10) **Patent No.: US 7,341,750 B2**
(45) **Date of Patent: Mar. 11, 2008**

(54) **COMPOUND ISOLATED FROM *GINKGO BILOBA* BARK, ISOLATION METHOD THEREOF AND ANTIPLATELET COMPOSITION CONTAINING THE SAME**

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(73) Assignee: **Candleflower Co., Ltd.**, Icheon (KR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **11/594,545**

(22) Filed: **Nov. 8, 2006**

(65) **Prior Publication Data**

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(30) **Foreign Application Priority Data**

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Jul. 14, 2006 (KR) 10-2006-0066085

(51) **Int. Cl.**
A61K 36/16 (2006.01)

(52) **U.S. Cl.** **424/752**
(58) **Field of Classification Search** ..... None
See application file for complete search history.

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* cited by examiner

Primary Examiner—Susan Hoffman
Assistant Examiner—Catheryne Chen
(74) *Attorney, Agent, or Firm*—John K. Park; Park Law Firm

(57) **ABSTRACT**

Disclosed herein are a novel compound isolated from *Ginkgo biloba* and a method for isolating the novel compound from *Ginkgo biloba*. The method comprises: (1) extracting *Ginkgo biloba* with alcohol to obtain a crude extract; (2) subjecting the *Ginkgo biloba* crude extract to solvent fractionation using an organic solvent; (3) fractionating the solvent fractions by Sephadex column chromatography; and (4) fractionating the Sephadex fractions by silica gel column chromatography.

8 Claims, 8 Drawing Sheets

minutes. The obtained PRP was separated into platelet-poor plasma (PPP) and platelets (PLTs). Then, concentrated PRP was prepared in the following manner. That is, platelets (PLTs) were suspended in a suitable amount of the supernatant PPP and measured for absorbance at 660 nm using a UV/visible spectrophotometer. Based on the measured absorbance, the suspension was further diluted with an excess of PPP to prepare concentrated PRP containing 5×10^8 platelets/ml. Herein, an OD value of 1.1 at 660 nm means 1×10^8 PLTs. A washing buffer used in the present invention was a pH 6.5 buffer containing 129 mM NaCl, 10.9 mM sodium citrate dihydrate, 8.9 mM $NaHCO_3$, 1 mg/ml glucose, 10 mM tris-hydroxymethylaminomethane, 2.8 mM KCl, 0.8 mM KH_2PO_4 and 2 mM EDTA. Also, a suspension buffer used in this test example was a pH 6.9 buffer, which was the same as said washing buffer, except that it contained no EDTA.

The platelet aggregation inhibitory effect of the novel compound was examined using the prepared concentrated PRP in the following manner. First, the concentrated PRP was used to make 500 μl of an in vitro reaction system. For use as a control group, the concentrated PRP was stabilized at 37° C. for 3 minutes and treated with collagen (Chrono-LogCo.) as a stimulating agent at a concentration of 10 μg/ml, and the aggregation of platelets in the reaction system was induced for 5 minutes. Meanwhile, the same reaction system as described above was treated with the novel compound, was allowed to react with the novel compound for 3 minutes, was stimulated with collagen for 6 minutes according to the same method as described above so as to induce platelet aggregation, and then was measured for aggregated platelets. The aggregation of platelets was measured with a change in light transmission using an aggregometer (Chrono-Log Co.) at 37° C. The measurement results are shown in Table 1 below and FIGS. **6**, **7** and **8**.

Table 1 summarizes the antiplatelet aggregation activities of aspirin, the novel compound and ginkgolide A and B against platelet aggregation factors, including ADP, collagen and arachidonic acid. As shown in Table 1, aspirin showed IC_{50} (half maximal inhibitory concentration) values of 316 μM and 203 μM against aggregation factors ADP and collagen, respectively, and the novel compound and ginkgolide A and B did not show an effect against the aggregation factor ADP, but showed IC_{50} values of 680, 482 and 480 μM, respectively, against collagen-stimulated platelet aggregation. In the case of the group treated with the novel compound, when arachidonic acid was used as the aggregation factor, the aggregation of platelets occurred only upon stimulation with 1,000 μM (i.e., 1 mM) or higher concentration of arachidonic acid. In the case of the groups treated with ginkgolide A and B, arachidonic acid-stimulated platelet aggregation did not occur.

FIG. **6** is a graphic diagram showing the inhibitory activity of aspirin on collagen-stimulated platelet aggregation. As shown in FIG. **6**, aspirin inhibited platelet aggregation in a concentration-dependent manner. FIG. **7** is a graphic diagram showing the inhibitory activity of the novel compound isolated from *Ginkgo biloba* on collagen-stimulated platelet aggregation. As shown in FIG. **7**, the novel compound inhibited collagen-stimulated platelet aggregation in a concentration-dependent manner. FIG. **8** is a graphic diagram showing the inhibitory effect of each of gingkolide A and B on collagen-stimulated platelet aggregation. As shown in FIG. **8**, each of gingkolide A and B inhibited collagen-stimulated platelet aggregation in a concentration-dependent manner.

TABLE 1

Antiplatelet aggregation activities of aspirin, novel compound and gingkolide A and B

Compounds	IC_{50} (μM) ADP	Collagen	AA
Aspirin	316	203	N.D
Novel compound	—	680	>1,000
Gingkolide A	—	482	—
Gingkolide B	—	480	—

N.D = not determined
—: no effect

As described above, it can be seen from said Example and Test Example that the inventive novel compound isolated from the *Ginkgo biloba* bark has antiplatelet activity. Thus, according to the present invention, the novel compound isolated from the *Ginkgo biloba* bark can be provided.

Also, the novel compound according to the present invention is a natural substance, and thus has no side effects caused by synthetic compounds. Also, the novel natural compound having antiplatelet aggregation activity can be extracted from the leaf or bark of *Ginkgo biloba* and used as a natural antithrombotic agent having collagen-stimulated platelet aggregation effects.

Moreover, the novel compound isolated from the *Ginkgo biloba* bark can inhibit thrombus formation induced by collagen.

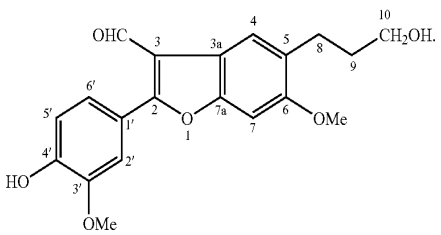
Furthermore, the novel compound can may inhibit serotonin secretion caused by collagen, which performs an important role in thrombus formation. Also, it can may inhibit the activity of guanylate cyclase acting as a mediator in a mediator in a signaling process associated with thrombus formation and inhibit an increase in intracellular calcium ions as secondary signaling substances of thrombus formation.

In addition, the inventive novel compound shows effects similar to those of gingkolide A and B, which have been used as antithrombotic compounds in the prior art. Thus, a composition containing the novel compound has excellent antithrombotic effects and can be used for the treatment of diseases, including arteriosclerosis, cerebral hemorrhage, cerebral stroke and cerebral infarction, which involve thrombosis.

Although the preferred embodiment of the present invention has been described for illustrative purposes, those skilled in the art will appreciate that various modifications, additions and substitutions are possible, without departing from the scope and spirit of the invention as disclosed in the accompanying claims.

What is claimed is:

1. A compound isolated from the bark of *Ginkgo biloba* and represented by the following formula:



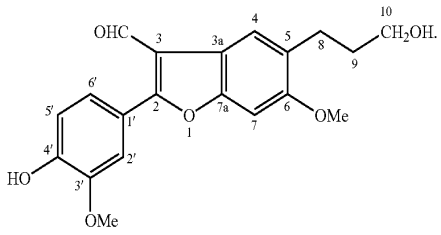
2. A method for isolating a compound represented by the following formula, the method comprising the steps of:

(1) extracting *Ginkgo biloba* with alcohol to obtain a crude extract;

(2) subjecting the *Ginkgo biloba* crude extract to solvent fractionation using an organic solvent;

(3) fractionating the solvent fractions by Sephadex column chromatography; and

(4) fractionating the Sephadex fractions by silica gel column chromatography:

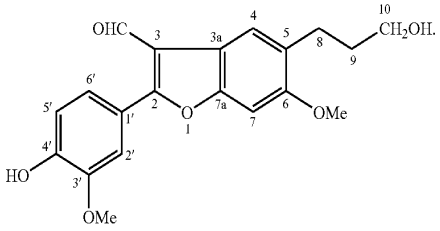


3. The method of claim 2, wherein the *Ginkgo biloba* used in said step (1) is any one selected from the bark, xylem, root and leaf of *Ginkgo biloba*, or a mixture of two or more thereof.

4. The method of claim 2, wherein the alcohol used in said step (1) is methanol, ethanol, or a mixture thereof.

5. The method of claim 2, wherein the organic solvent is selected from the group consisting of light petroleum ether (LPE), methylene chloride (CH_2Cl_2), ethyl acetate (EtOAc), and mixtures thereof.

6. An antiplatelet composition containing a compound of the following formula, said compound being isolated from the bark of *Ginkgo biloba* and acting as an inhibitor against collagen-stimulated platelet aggregation:



7. The composition of claim 6, which is in the form of a pharmaceutical preparation, which can be administered orally or parenterally.

8. The composition of claim 6, wherein the pharmaceutical preparation is prepared in the form of a powder, a granule, a tablet, a capsule or an injection solution by mixing the compound with a pharmaceutically acceptable carrier, excipient or diluent.

* * * * *

Exhibit 28

US007307057B2

(12) **United States Patent**
Lazzarini et al.

(10) **Patent No.: US 7,307,057 B2**
(45) **Date of Patent: *Dec. 11, 2007**

(54) **ANTIBIOTIC 107891, ITS FACTORS A1 AND A2, PHARMACEUTICALLY ACCEPTABLE SALTS AND COMPOSITIONS, AND USE THEREOF**

(75) Inventors: **Ameriga Lazzarini**, Legnano (IT); **Luciano Gastaldo**, Pogliano Milanese (IT); **Gianpaolo Candiani**, Gorgonzola (IT); **Ismaela Ciciliato**, Busto Arsizio (IT); **Daniele Losi**, Rovellasca (IT); **Flavia Marinelli**, Milan (IT); **Enrico Selva**, Gropello Cairoli (IT); **Franco Parenti**, Lainate (IT)

(73) Assignee: **Naicons S.C.A.R.L.**, Milan (IT)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **10/521,336**

(22) PCT Filed: **Jul. 12, 2004**

(86) PCT No.: **PCT/EP2004/007658**

§ 371 (c)(1),
(2), (4) Date: **Jan. 20, 2006**

(87) PCT Pub. No.: **WO2005/014628**

PCT Pub. Date: **Feb. 17, 2005**

(65) **Prior Publication Data**

US 2006/0183673 A1 Aug. 17, 2006

(30) **Foreign Application Priority Data**

Jul. 18, 2003 (EP) 03016306

(51) **Int. Cl.**
A61K 38/04 (2006.01)

(52) **U.S. Cl.** **514/2**

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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Primary Examiner—Cecilia J. Tsang
Assistant Examiner—Christina M. Bradley
(74) *Attorney, Agent, or Firm*—Arthur R. Crawford; Charles W. Ashbrook; John H. Engelmann

(57) **ABSTRACT**

The invention relates to an antibiotic substance of microbial origin, arbitrarily denominated antibiotic 107891 which is produced by fermentation of *Microbispora* sp. ATCC PTA-5024, the pharmaceutically acceptable salts and compositions thereof, and their use as an antibacterial agent having inhibitory activity versus susceptible microbes.

Antibiotic 107891 and its Factors A1 and A2 show a good antibacterial activity against Gram-positive bacteria including methicillin resistant and vancomycin resistant strains, and is active also against some Gram-negative bacteria such as *M. catharralis, Neisseria* species and *H. influenzae* and *Mycobacteria.*

21 Claims, 18 Drawing Sheets

-continued

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cgacgccgcg tgggggatga cggccttcgg gttgtaaacc tctttcagca gggacgaagt    420

tgacgtgtac ctgtagaaga agcgccggct aactacgtgc cagcagccgc ggtaatacgt    480

agggcgcaag cgttgtccgg aattattggg cgtaaagagc tcgtaggtgg cttgttgcgt    540

ctgccgtgaa agcccgtggc ttaactacgg gtctgcggtg gatacgggca ggctagaggc    600

tggtaggggc aagcggaatt cctggtgtag cggtgaaatg cgcagatatc aggaggaaca    660

ccggtggcga aggcggcttg ctgggccagt tctgacgctg aggagcgaaa gcgtggggag    720

cgaacaggat tagataccct ggtagtccac gctgtaaacg ttgggcgcta ggtgtggggg    780

tcttccacga ttcctgtgcc gtagctaacg cattaagcgc cccgcctggg gagtacggcc    840

gcaaggctaa aactcaaagg aattgacggg ggcccgcaca agcggcggag catgttgctt    900

aattcgacgc aacgcgaaga accttaccaa ggtttgacat acaccggaaa gctctggaga    960

cagggccctc ctttggactg gtgtacaggt ggtgcatggc tgtcgtcagc tcgtgtcgtg   1020

agatgttggg ttaagtcccg caacgagcgc aacccttgtt ccatgttgcc agcacgccct   1080

ttggggtggt ggggactcat gggagactgc cggggtcaac tcggaggaag gtggggatga   1140

cgtcaagtca tcatgccccc tatgtcttgg gctgcaaaca tgctacaatg gtcggtacag   1200

agggttgcga tgccgtgagg tggagcgaat ccctaaaagc cggtctcagt tcggattggg   1260

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cgaagcccgt ggcccaacca cttgtggggg gagcggtcga aggtggggct ggcgattggg   1440

acg                                                                1443
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The invention claimed is:

1. Antibiotic 107891 complex, isolated from *Microbispora* sp. ATCC PTA-5024, comprising Factor A1 and Factor A2 being a white powder having the following characteristics:

(A) Mass spectrum recorded from a 0.2 mg/nil solution in methanol:water 80/20 (v/v) with trifluoracetic acid 0.1% on a Thermofinnigan LCQ deca instrument fitted with an electrospray source, using Thermofinnigan calibration mix under the following electrospray conditions: spray voltage: 4.7 kV; capillary temperature: 220.degree. C.; capillary voltage: 3V; infusion mode 10.mu.l/min, showing two double protonated ions at m/z 1124 and nih 1116, corresponding to the lowest isotope composition of Factor A1 and A2, respectively;

(B) Infrared spectrum recorded in KBr with a Bruker FT-IR spectophotometer model IFS 48, exhibiting absorption maxima at (cm^{-1}) 3263; 2929; 1661; 1533; 1402; 1114; 1026;

C) U.V. spectrum perfommed in methanol:H 2080:20 (v/v) with a Perkin-Elmer spectrophotometer Lambda 16, exhibiting two shoulders at 226 and 267 nm;

D) ^{1}H-NMR spectrum recorded at 600 MHz in the mixture methanol-d4:$H^{2}O$ (pH 4.3 HCl) 40:10 (v/v) at 40 degrees C. on a Bruker AMX 600 spectrometer applying a water suppression sequence using as internal standard the residual signal of methanol-d4 at 3.31 ppm, exhibiting the following signals [δ=ppm muliplicity; (attribution)]:0.93 d (CH_3), 0.98 d (CH_3), 1.07 t (overlapped CH_3's), 1.18 t (overlapped CH_3's), 1.26 s (CH_3), 1.30 t (overlapped CH_3's), 1.62-1.74 m (CH_2), 1.78 d (CH_3), 1.80 d (CH_3), 2.03 m (CH_2), 2.24 m (CH), 2.36 m (CH_2), 2.72-3.8 m (peptidic alpha CH's), 3.8-5.2 m (peptidic alpha CH's), 5.53-6.08 s (CH_2), 5.62 d (CH double bond), 6.42 m (CH), 6.92 d (CH double bond), 7.0-7.55 m (aromatic CH's), 7.62-10.4 d and m (aromatic and peptidic NH's);

E) ^{13}C-NMR spectrum recorded in the mixture methanol-d4:H2O (pH 4.3 HCl) 40:10 (v/v) at 40 degrees C. on a Bruker AMX 600 spectrometer, using as internal standard the residual signal of methanol-d4 at 49.15 ppm, exhibiting the following signals: [δ=ppm; (attribution)]: 13.6-23.2 (aliphatic CH_3's), 26.16-73 (aliphatic CH_2's and peptidic alpha CH's), 105-136 (aromatic and double bonds CH's and quartenary carbons), 164.3-176.3 (peptidic carbonyls);

F) the acid hydrolysate in 6N HCl, (105 degrees C., 24 h) showing the presence of the following amino acids, along with other unidentified peaks, after derivatization with 6-aminoquinolyl-N-hydroxysuccinmmidyl carbamate: lanthionine, methyllanthionine, glycine, proline, valine, aspartic acid (hydrolysis product of asparagine), phenylalanine and leucine;

G) the acid hydrolysate in 4N methanesulfonic acid containing 0.2% (w/v) 3-(2-aminoethyl) indole as catalyst (115 degrees C., 16 h) showing the presence of 5-chlorotryptophan; and

H) a basic ionizable function detected by acid/base titration performed with 0.01 N potassium hydroxide in 2-methoxyethanol (MCS):H_2O 12:3 (v/v) containing a molar excess of 0.01 N hydrochloric acid.

2. Antibiotic 107891 Factor A1, isolated from *Microbispora* sp. ATCC PTA-5024, being a white powder having the following characteristics:

A) a doubly protonated ion at m/z 1124 corresponding to the lowest isotope composition in mass spectrum

recorded from a 0.1 mg/ml solution in acetonitrile: water 50:50 (v/v) with acetic acid 0.5% on a Thermofinnigan LCQ deca instrument fitted with an electrospray source, using Thermofinnigan calibration mix under the following electrospray conditions: spray voltage: 4.7 kV; capillary temperature; 250.degree. C.; capillary voltage: 8V; infusion mode 10 μl/min;

B) the exact mass of antibiotic determined by using a Bruker Daltonics APEX II, 4.7 Tesla spectrometer fitted with an electrospray source, corresponding to a molecular weight of 2246.71±0.06, calculated monoisotopic mass from $[M+2H]^{2+}$ at m/z 1124.36124 (accuracy 30 ppm);

C) when dissolved in $CD_3CN:D_2O$ (1:1), ^1H NMR spectrum exhibiting the following groups of signals (in ppm) at 600 MHz using CD_3CN as internal standard (1.94 ppm). [δ=ppm, multiplicity; (attribution)]: 0.84 d (CH_3), 0.89 d (CH_3). 0.94 t (overlapped CH_3s), 1.1 d (CH_3), 1.13 d (CH_3), 1.15 t (overlapped CHH_3's), 149 m (CH_2). 1.69 d (CH_3). 1.75 m (CH_2), 2.11 m (CH), 2.26 m (CH), 2.5 m (CH_3), 2.68-3.8 m (peptidic CH_β's), 3.8-5.0 m (peptidic CH_α's), 5.45-6.17 s (CH_2), 5.58 d (CH double bond), 6.36 m (CH), 6.86 d (CH double bond), 7.0-7.45 m aromatic CH's);

D) when dissolved in $CD_3CN:D_2O$ (1:1), .sup.^{13}C NMR spectrum exhibiting the following signals (in ppm) at 600 MHz using CD_3CN as internal standard (1.39 ppm), [δ=ppm; (attribution)]: 13.6-23.03 (aliphatic CH_3's), 25.69-77.9 (aliphatic CH_2's and peptidic $_\alpha$'s), 105-137.3 (aromatic and double bonds CH's and quaternary carbons), 165.6-176.6 (peptidic carbonyls);

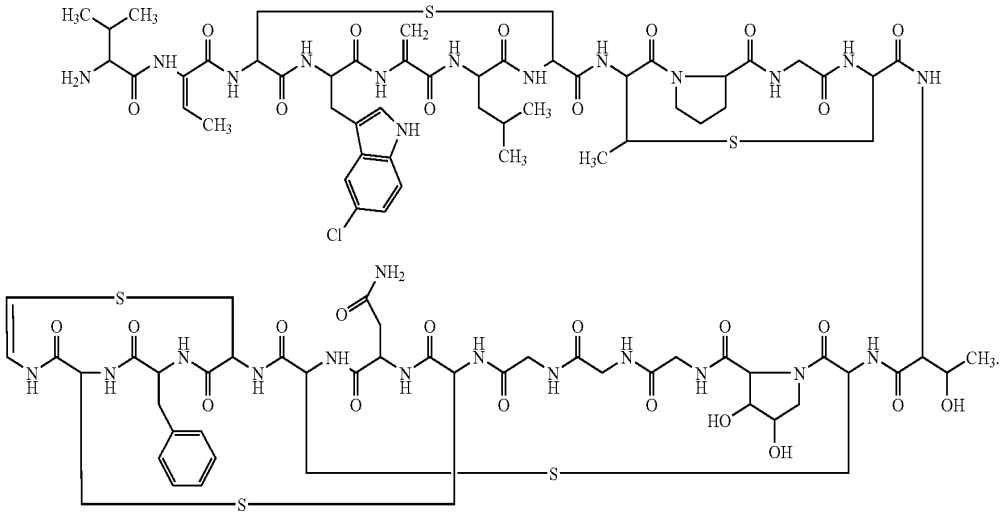
E) Infrared spectrum recorded in KBr with a Bruker FT-IR spectophotometer model IFS 48 exhibiting absorption maxima at (cm^{-1}): 3294; 3059; 2926; 1661; 1529; 1433; 1407; 1287; 1114; 1021;

F) U.V. spectrum recorded in rnethanol:H_2O (in ratio 80:20) with a Perkin-Elmer spectrophotometer Lambda 16 exhibiting two shoulders at 226 and 267 nm;

G) The acid hydrolysate in 6N HCl, (105 degrees C., 24 h) showing the presence of the following amino acids, along with other unidentified peaks, after derivatization with 6-aminoquinolyl-N-hydroxysuccinimidyl carbamate: lanthionine, methyllanthionine, glycine, pro line, valine, aspartic acid (hydrolysis product of asparagine), phenylalanine, and leucine; and

H) the acid hydrolysate in 4N methanesulfonic acid containing 0.2% (w/v) 3-(2-aminoethyl)indole as catalyst (115 degrees C., 16 h) showing the presence of 5-chlorotryptophan.

3. The antibiotic 107891 Factor A1 of claim **2**, having the following structural formula:



4. Antibiotic 107891 Factor A2, isolated from *Microbispora* sp. ATCC PTA-5024, being a white powder having the following characteristics:

A) a doubly protonated ion at m/z 1116 corresponding to the lowest isotope composition in mass spectrum recorded from a 0.1 mg/ml solution in acetonitrile: water 50:50 (v/v) with acetic acid 0.5% on a Thermofinnigan LCQ deca instrument fitted with an electrospray source, using Thermofmnigan calibration mix under the following electrospray conditions: spray voltage: 4.7 kV; capillary temperature: 250 degrees C.; capillary voltage: 8V; infusion mode 10 μl/min;

B) the exact mass determined by using a Bruker Daltonics APEX II, 4.7 Tesla spectrometer fitted with an electrospray source, corresponding to a molecular weight of 2230.71.+-.0.06, calculated monoisotopic mass from $[M+2H]^2+$ at m./z 1116.36260 (accuracy 30 ppm);

(C) when dissolved in $CD_3CN:D_2O$ (1:1), .sup.1H NMR spectrum exhibiting the following signals (in ppm) at 600 MHz using CD_3CN as internal standard (1.94 ppm), [δ=ppm, multiplicity; (attribution)]: 0.84 d (CH_3), 0.88 d (CH_3), 0.94 d (CH_3), 1.06 d (CH_3), 1.14 d (CH_3), 148 m(CH_2), 1.65-1.75 m (CH_2), 1.67 d (CH_3), 2.15 m (CH), 2.25 m (CH), 2.5 m (CH_2), 2.77-3.8 m (peptidic CH_β's), 3.8-4.9 m (peptidic CH .alpha.'s), 5.45-6.14 s(CH_2), 5.59 d (CH double bond), 6.34 m (CH), 6.84 d (CH double bond), 7.0-7.42 m (aromatic CH's);

D) when dissolved in $CD_3CN:D_2O$ (1:1), ^{13}C NMR spectrum exhibiting the following signals (in ppm) at 600 MHz using CD $_3$CN as internal standard (1.39

ppm), [δ=ppm; (attribution)]: 13.6-22.9 (aliphatic CH_3's), 25.65-73 (aliphatic CH_2's and peptidic CH_α's), 105-137.3 (aromatic and double bonds CH's and quaternaiy carbons). 165.7-176.1 (peptidic carbonyls);

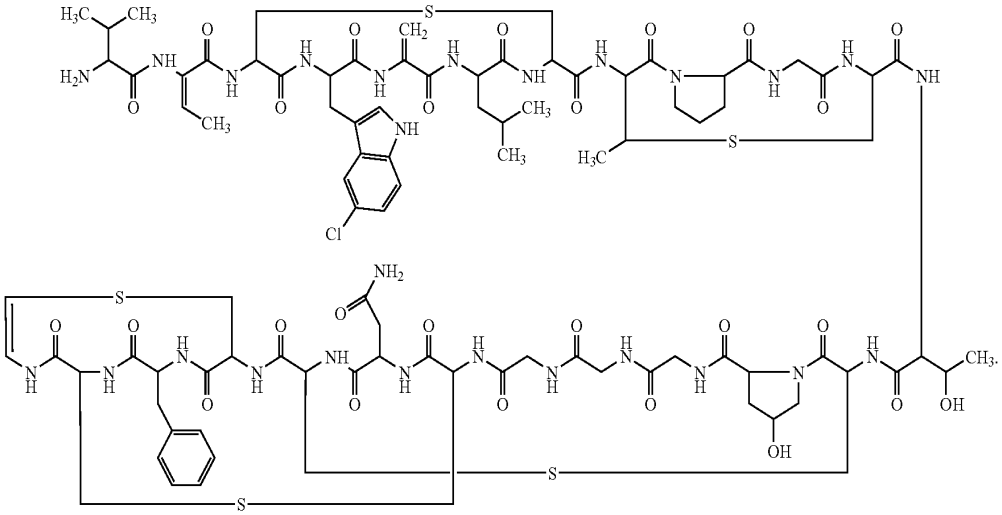
E) infrared spectrum recorded in KBr with a Bruker FT-IR spectophotometer model IFS 48, exhibiting absorption maxima at (cm^{-1}): 3296; 3060; 2928; 1661; 1529; 1433; 1407; 1288; 1116;

F) U.V. spectrum recorded in methanol :H_2O (in ratio 80:20) with a Perkin-Elmer spectrophotometer Lambda 16 exhibiting two shoulders at 226 and 267 nm;

G) the acid hydrolysate in 6N HCl, (105° C., 24 h) showing the presence of the following amino acids, along with other unidentified peaks, after derivatization with 6-aminoquinolyl-N-hydroxysuccinimidyl carbamate: lanthionine, methyllanthionine, glycine, proline, valine, aspartic acid (hydrolysis product of asparagine), phenylalanine and leucine; and

H) the acid hydrolysate in 4N methanesulfonic acid containing 0.2% (w/v) 3-(2-aminoethyl)indole as catalyst (115° C., 16 h) showing the presence 5-chiorotryptophan.

5. The antibiotic 107891 Factor A2 of claim **4** having the following structural formula:



6. A process for producing antibiotic 107891, isolated from *Microbispora* sp. ATCC PTA-5024 and its Factors A1 and A2 and the salts thereof, comprising the steps of: cultivating *Microbispora*. sp. ATCC PTA-5024 or a variant or mutant thereof maintaining the ability to produce said antibiotic, under aerobic conditions, in an aqueous nutrient medium containing an assimilable source of carbon, nitrogen and inorganic salts; isolating the resulting antibiotic from the mycelium and/or the filtered fermentation broth; and purifying the isolated antibiotic 107891.

7. The process according to claim **6**, wherein the strain *Microbispora* sp. ATCC PTA-5024 or the antibiotic 107891 producing variant or mutant are pre-cultured.

8. The process according to claim **6**, wherein the isolation of the antibiotic 107891 is carried out by filtering the fermentation broth and the antibiotic is recovered from the filtered fermentation broth according to a technique selected from the group consisting of: extraction with a water-immiscible solvent, precipitation by adding a non-solvent or by changing the pH of the solution, absorption chromatography, partition chromatography, reverse phase partition chromatography, ion exchange chromatography, molecular exclusion chromatography, and a combination of two or more of said techniques.

9. The process according to claim **6**, wherein the isolation of the antibiotic 107891 is carried out by separating the mycelium from the supernatant of the fermentation broth and extracting the mycelium with a water-miscible solvent whereby, after the removal of the spent mycelium, a water-miscible solution containing the crude antibiotic is obtained, which can be processed either separately or in pool with the filtered fermentation broth to recover the antibiotic 107891 by means of a technique selected from the group consisting of: extraction with a solvent, precipitation by adding a non-solvent or by changing the pH of the solution, absorption chromatography, partition chromatography, reverse phase partition chromatography, ion exchange chromatography and molecular exclusion chromatography, and a combination of two or more of said techniques.

10. The process according to claim **9**, wherein the concentration of the water-miscible solvent in the mycelium extract is reduced before it is processed to recover the antibiotic therefrom.

11. The process according to claim **8**, wherein the filtered fermentation broth is contacted with an absorption resin, and said resin is eluted with a polar, water-miscible solvent or a mixture thereof with water, whereby a solution containing the crude antibiotic 107981 is obtained.

12. The process according to claim **11**, wherein the absorption resin is selected from the group consisting of a polystyrene, a mixed polystyrene-divinylbenzene, and a polyamide resin.

13. The process according to claim **9**, wherein the mycelium is extracted with a C1-C3 alkanol, and the mycelium extract is contacted with an absorption resin, and eluted therefrom with a polar water-miscible solvent or a mixture

thereof with water, whereby a solution containing the crude antibiotic 107891 is obtained.

14. The process according to claim **13**, wherein the solutions containing the crude antibiotic 107891 are pooled and processed for further purification of said antibiotic 107891.

15. The process according to claim **13**, wherein the solution containing the crude antibiotic 107981 is concentrated and then freeze-dried to yield a crude antibiotic 107891 solid product.

16. The process according to claim **11**, wherein the absorption resins containing the absorbed antibiotic are pooled and their mixture is eluted with a polar, water-miscible solvent or a mixture thereof with water.

17. The process according to claim **6**, wherein the antibiotic 107981 is purified by means of a chromatographic procedure.

18. The process according to claim **17**, wherein the chromatographic procedure is selected from the group consisting of preparative HPLC and medium pressure chromatography.

19. The process according to claim **6**, wherein Factor A1 and Factor A2 are separated by preparative HPLC from the purified antibiotic 107891.

20. A phannaceutical composition comprising an antibiotic selected from the group consisting of: antibiotic 107891, antibiotic 107891 Factor A1, antibiotic 107891 Factor A2, and a mixture of said Factors in any proportion or a pharmaceutically acceptable salt thereof with an acid.

21. The pharmaceutical composition according to claim **20**, further comprising a pharmaceutically acceptable carrier.

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