

## (12) 按照专利合作条约所公布的国际申请

(19) 世界知识产权组织  
国际局

(43) 国际公布日  
2016 年 7 月 21 日 (21.07.2016)



(10) 国际公布号  
WO 2016/112875 A3

(51) 国际专利分类号:

C07C 69/16 (2006.01) A61K 31/222 (2006.01)  
C07C 69/40 (2006.01) A61K 31/192 (2006.01)  
C07C 65/105 (2006.01) A61K 31/223 (2006.01)  
C07C 229/08 (2006.01) A61K 31/05 (2006.01)  
C07C 39/15 (2006.01) A61P 25/28 (2006.01)

(21) 国际申请号: PCT/CN2016/076124

(22) 国际申请日: 2016 年 3 月 11 日 (11.03.2016)

(25) 申请语言: 中文

(26) 公布语言: 中文

(30) 优先权:  
201510016733.9 2015 年 1 月 13 日 (13.01.2015) CN

(71) 申请人: 西安力邦制药有限公司 (XI'AN LIBANG PHARMACEUTICAL CO., LTD) [CN/CN]; 中国陕西省西安市高新二路 18 号, Shaanxi 710075 (CN)。

(72) 发明人: 王汝涛 (WANG, Rutao); 中国陕西省西安市高新二路 18 号, Shaanxi 710075 (CN)。 陈涛 (CHEN, Tao); 中国陕西省西安市高新二路 18 号, Shaanxi 710075 (CN)。 安龙 (AN, Long); 中国陕西省西安市高新二路 18 号, Shaanxi 710075 (CN)。 赵熠 (ZHAO, Yi); 中国陕西省西安市高新二路 18 号, Shaanxi 710075 (CN)。 王惟娇 (WANG, Weijiao); 中国陕西省西安市高新二路 18 号, Shaanxi 710075 (CN)。

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(74) 代理人: 北京三友知识产权代理有限公司 (BEIJING SANYOU INTELLECTUAL PROPERTY AGENCY LTD.); 中国北京市金融街 35 号国际企业大厦 A 座 16 层, Beijing 100033 (CN)。

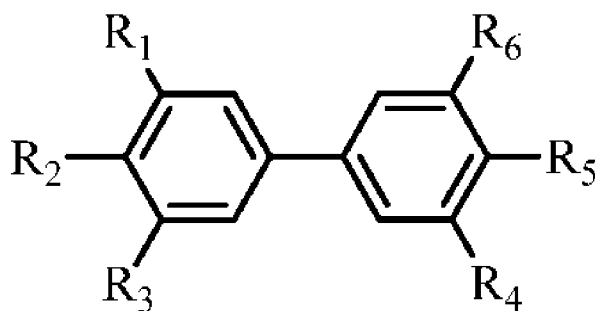
(81) 指定国 (除另有指明, 要求每一种可提供的国家保护): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW。

(84) 指定国 (除另有指明, 要求每一种可提供的地区保护): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), 欧亚 (AM, AZ, BY, KG, KZ, RU, TJ, TM), 欧洲 (AL, AT, BE, BG, CH,

[见续页]

(54) Title: DIPHENYL DERIVATIVE AND USES THEREOF

(54) 发明名称: 二联苯衍生物及其应用



(I)

(57) Abstract: The present invention relates to a diphenyl derivative and uses thereof, the diphenyl derivative having the structure as indicated in formula (I) defined in the description. The uses refer to the uses of the diphenyl derivative, pharmaceutical salts thereof, solvates thereof, or pharmaceutical compositions containing said diphenyl derivative, pharmaceutical salts thereof, or solvates thereof in the preparation of medicines for the prevention and/or treatment of cerebral ischemia.

(57) 摘要: 本发明涉及二联苯衍生物及其应用, 所述二联苯衍生物具有如说明书所定义的式(I)所示的结构。所述应用是指所述二联苯衍生物或其药用盐、溶剂化物, 或包含所述二联苯衍生物或其药用盐、溶剂化物的药物组合物在制备治疗和/或预防缺血性脑卒中的药物中的应用。



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CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE,  
IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO,  
RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI,  
CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD,  
TG)。

— 包括关于请求恢复一项或多项优先权要求的信息  
(细则 26 之二.3 和 48.2(b)(vii))。

(88) 国际检索报告公布日期: 2016 年 9 月 9 日

**本国际公布:**

— 包括国际检索报告(条约第 21 条(3))。

# INTERNATIONAL SEARCH REPORT

International application No.

**PCT/CN2016/076124**

## A. CLASSIFICATION OF SUBJECT MATTER

C07C 69/16 (2006.01) i; C07C 69/40 (2006.01) i; C07C 65/105 (2006.01) i; C07C 229/08 (2006.01) i; C07C 39/15 (2006.01) i; A61K 31/222 (2006.01) i; A61K 31/192 (2006.01) i; A61K 31/223 (2006.01) i; A61K 31/05 (2006.01) i; A61P 25/28 (2006.01) i  
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)

C07C, A61K, A61P

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

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

CNABS, CNKI, DWPI, SIPOABS, CAPLUS, REG, biphenyl, phenol, stroke, propofol, peroxidation, antioxidant, bisphenol, brain, ischemia, cerebral apoplexy, cerebralapoplexy, structure search based on claim1

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                        | Relevant to claim No. |
|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| PX        | CN 104557532 A (XI'AN LIBANG PHARMACEUTICAL CO., LTD.), 29 April 2015 (29.04.2015), the whole document                                                                                                                                    | 1-18                  |
| PX        | CN 104546809 A (XI'AN LIBANG PHARMACEUTICAL CO., LTD.), 29 April 2015 (29.04.2015), the whole document                                                                                                                                    | 1-18                  |
| X         | CN 101006094 A (SHARP KABUSHIKI KAISHA), 25 July 2007 (25.07.2007), description, page 27, structural formula                                                                                                                              | 1-3, 8, 9             |
| X         | THI, T.H.D. et al., "Pre-Treatment with the Synthetic Antioxidant T-Butyl Bisphenol Protects Cerebral Tissues from Experimental Ischemia Reperfusion Injury", JOURNAL OF NEUROCHEMISTRY, vol.130, 31 December 2014 (31.12.2014), abstract | 1-18                  |
| X         | SHIGERU, S. et al., "Synthesis of Crowded Triarylphosphines Carrying Functional Sites", JOURNAL OF ORGANOMETALLIC CHEMISTRY, vol.690, 30 November 2004 (30.11.2004), page 2666                                                            | 1-5, 8, 9             |

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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

|                                                                                                                                                                                                                    |                                                                                        |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Date of the actual completion of the international search<br>07 June 2016 (07.06.2016)                                                                                                                             | Date of mailing of the international search report<br><b>15 June 2016 (15.06.2016)</b> |
| Name and mailing address of the ISA/CN:<br>State Intellectual Property Office of the P. R. China<br>No. 6, Xitucheng Road, Jimenqiao<br>Haidian District, Beijing 100088, China<br>Facsimile No.: (86-10) 62019451 | Authorized officer<br><b>WANG, Ying</b><br>Telephone No.: (86-10) <b>62084463</b>      |

**INTERNATIONAL SEARCH REPORT**

International application No.

**PCT/CN2016/076124****C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                 | Relevant to claim No. |
|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | SAMUEL, C.T. et al., "Polymers from Bisphenols. Steric Inhibition of Condensation Polymerization", THE JOURNAL OF ORGANIC CHEMISTRY, vol.26, 31 December 1961 (31.12.1961), page 2519, the first formula and the definition of R, R1, R2 and R3 by No.4 compound in the table                                                                                      | 1-3, 8, 9             |
| X         | PRADIP, K. et al., "Fully Aromatic Thermotropic Liquid Crystalline Polyesters of Substituted 4, 4'-Biphenols. IV. Homopolyesters with Terephthalic Acid and Copolyesters with Terephthalic Acid and 4-Hydroxybenzoic Acid", JOURNAL OF POLYMER SCIENCE: PART A: POLYMER CHEMISTRY, vol.31, 31 December 1993 (31.12.1993), page 2116, left-hand column, paragraph 3 | 1-3, 6, 8, 9          |

## INTERNATIONAL SEARCH REPORT

International application No.

**PCT/CN2016/076124**

### **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. ☒ Claims Nos.: 19 and 20  
because they relate to subject matter not required to be searched by this Authority, namely:  
[1]     the subject matter of claims 19 and 20 is a method for treating a disease, which falls within the subject matter for which a search is not required by the International Searching Authority defined in PCT Rule 39.1.
2. ☐ Claims Nos.:  
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:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

International application No.  
**PCT/CN2016/076124**

Form PCT/ISA/210 (patent family annex) (July 2009)

| <b>A. 主题的分类</b><br>C07C 69/16(2006.01)i; C07C 69/40(2006.01)i; C07C 65/105(2006.01)i; C07C 229/08(2006.01)i;<br>C07C 39/15(2006.01)i; A61K 31/222(2006.01)i; A61K 31/192(2006.01)i; A61K 31/223(2006.01)i; A61K<br>31/05(2006.01)i; A61P 25/28(2006.01)i<br>按照国际专利分类(IPC)或者同时按照国家分类和IPC两种分类                                                                                                                              |                                                                                                                                                                                                                                         |                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| <b>B. 检索领域</b><br>检索的最低限度文献(标明分类系统和分类号)<br>C07C, A61K, A61P<br>包含在检索领域中的除最低限度文献以外的检索文献<br>在国际检索时查阅的电子数据库(数据库的名称, 和使用的检索词(如使用))<br>CNABS, CNKI, DWPI, SIPOABS, CAPLUS, REG, 联苯, 酚, 脑卒中, 丙伯酚, 缺血, 过氧化, antioxidant,<br>bisphenol, brain, ischemia, cerebral apoplexy, cerebralapoplexy, 基于权利要求1的结构检索                                                                                                                       |                                                                                                                                                                                                                                         |                                    |
| <b>C. 相关文件</b>                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                         |                                    |
| 类 型*                                                                                                                                                                                                                                                                                                                                                                                                                     | 引用文件, 必要时, 指明相关段落                                                                                                                                                                                                                       | 相关的权利要求                            |
| PX                                                                                                                                                                                                                                                                                                                                                                                                                       | CN 104557532 A (西安力邦制药有限公司) 2015年 4月 29日 (2015 - 04 - 29)<br>全文                                                                                                                                                                         | 1-18                               |
| PX                                                                                                                                                                                                                                                                                                                                                                                                                       | CN 104546809 A (西安力邦制药有限公司) 2015年 4月 29日 (2015 - 04 - 29)<br>全文                                                                                                                                                                         | 1-18                               |
| X                                                                                                                                                                                                                                                                                                                                                                                                                        | CN 101006094 A (夏普株式会社) 2007年 7月 25日 (2007 - 07 - 25)<br>说明书第27页结构式                                                                                                                                                                     | 1-3, 8, 9                          |
| X                                                                                                                                                                                                                                                                                                                                                                                                                        | THI T.H.D. 等. "Pre-treatment with the synthetic antioxidant T-butyl<br>bisphenol protects cerebral tissues from experimental ischemia reperfusion<br>injury"<br>Journal of Neurochemistry, 第130卷, 2014年 12月 31日 (2014 - 12 - 31),<br>摘要 | 1-18                               |
| X                                                                                                                                                                                                                                                                                                                                                                                                                        | SHIGERU S. 等. "Synthesis of crowded triarylphosphines carrying functional<br>sites"<br>Journal of Organometallic Chemistry, 第690卷, 2004年 11月<br>30日 (2004 - 11 - 30),<br>第2666页                                                         | 1-5, 8, 9                          |
| <input checked="" type="checkbox"/> 其余文件在C栏的续页中列出。 <input checked="" type="checkbox"/> 见同族专利附件。                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                         |                                    |
| * 引用文件的具体类型:<br>"A" 认为不特别相关的表示了现有技术一般状态的文件<br>"E" 在国际申请日的当天或之后公布的在先申请或专利<br>"L" 可能对优先权要求构成怀疑的文件, 或为确定另一篇引用文件的<br>公布日而引用的或者因其他特殊理由而引用的文件(如具体<br>说明的)<br>"O" 涉及口头公开、使用、展览或其他方式公开的文件<br>"P" 公布日先于国际申请日但迟于所要求的优先权日的文件<br>"T" 在申请日或优先权日之后公布, 与申请不相抵触, 但为了理解<br>发明之理论或原理的在后文件<br>"X" 特别相关的文件, 单独考虑该文件, 认定要求保护的发明不是<br>新颖的或不具有创造性<br>"Y" 特别相关的文件, 当该文件与另一篇或者多篇该类文件结合并<br>且这种结合对于本领域技术人员为显而易见时, 要求保护的发<br>明不具有创造性<br>"&" 同族专利的文件 |                                                                                                                                                                                                                                         |                                    |
| 国际检索实际完成的日期<br>2016年 6月 7日                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                         | 国际检索报告邮寄日期<br>2016年 6月 15日         |
| ISA/CN的名称和邮寄地址<br>中华人民共和国国家知识产权局(ISA/CN)<br>中国北京市海淀区蓟门桥西土城路6号 100088<br>传真号 (86-10)62019451                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                         | 受权官员<br>王影<br>电话号码 (86-10)62084463 |

| C. 相关文件 |                                                                                                                                                                                                                                                                                                                                         |              |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| 类 型*    | 引用文件, 必要时, 指明相关段落                                                                                                                                                                                                                                                                                                                       | 相关的权利要求      |
| X       | SAMUEL C. T. 等. "Polymers from Bisphenols. Steric Inhibition of Condensation Polymerization"<br>The Journal of Organic Chemistry, , 第26卷, 1961年 12月<br>31日 (1961 - 12 - 31),<br>第2519页第一个结构式及表格中No. 4化合物对R、R1、R2和R3的定义                                                                                                                  | 1-3, 8, 9    |
| X       | Pradip K. 等. "Fully Aromatic Thermotropic Liquid Crystalline Polyesters of Substituted 4, 4'-Biphenols. IV. Homopolyesters with Terephthalic Acid and Copolyesters with Terephthalic Acid and 4-Hydroxybenzoic Acid"<br>Journal of Polymer Science: Part A: Polymer Chemistry, 第31卷, 1993年 12月<br>31日 (1993 - 12 - 31),<br>第2116页左侧栏第3段 | 1-3, 6, 8, 9 |

第II栏

某些权利要求被认为是不能检索的意见(续第1页第2项)

根据条约第17条(2)(a)，对某些权利要求未做国际检索报告的理由如下：

1. ☒ 权利要求： 19, 20  
因为它们涉及不要求本单位进行检索的主题，即：  
[1] 权利要求19, 20的主题为疾病的治疗方法，其属于细则39.1定义的不要求国际检索单位检索的主题。
2. ☐ 权利要求：  
因为它们涉及国际申请中不符合规定的要求的部分，以致不能进行任何有意义的国际检索， 具体地说：
3. ☐ 权利要求：  
因为它们是从属权利要求，并且没有按照细则6.4(a)第2句和第3句的要求撰写。

国际检索报告  
关于同族专利的信息

国际申请号

PCT/CN2016/076124

| 检索报告引用的专利文件 |           |   | 公布日<br>(年/月/日) | 同族专利 | 公布日<br>(年/月/日) |
|-------------|-----------|---|----------------|------|----------------|
| CN          | 104557532 | A | 2015年 4月 29日   | 无    |                |
| CN          | 104546809 | A | 2015年 4月 29日   | 无    |                |
| CN          | 101006094 | A | 2007年 7月 25日   | 无    |                |