(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 November 2020 (26.11.2020)

WIPO | PCT

(10) International Publication Number
WO 2020/237247 A1

(51) International Patent Classification:
A61K 31/01 (2006.01) *A61K 31/045* (2006.01)
A61K 31/015 (2006.01)

(21) International Application Number:
PCT/US2020/034602

(22) International Filing Date:
26 May 2020 (26.05.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/852,257 23 May 2019 (23.05.2019) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: 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, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, 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).

Published:
— *with international search report (Art. 21(3))*

WO 2020/237247 A1

(54) Title: COMPOSITIONS AND METHODS USING CANNABINOIDS FOR TREATING STAMMERING/STUTERING AND SYMPTOMS OF TOURETTE SYNDROME

(57) Abstract: This invention relates to compositions and methods for treating stammering/stuttering and Tourette syndrome (TS) in humans, using a formulation comprising of a combination of a cannabis compound, or compounds.

COMPOSITIONS AND METHODS USING CANNABINOIDS FOR TREATING STAMMERING/STUTTERING AND SYMPTOMS OF TOURETTE SYNDROME

Summary

This invention relates to compositions and methods for treating stammering/ stuttering and Tourette syndrome (TS) in humans, using a formulation comprising of a combination of a cannabis compound, or compounds.

Background

Stuttering is a common speech disorder in persons of all ages that can be a basis for disturbances in the normal fluency and time patterning of speech. Recent evidence indicates that the disorder origin may be a result of inborn central nervous system abnormalities that interrupt fluent speech (Costa D and Kroll R, Review Shuttering: an update for physicians. CMAJ. 2000 Jun 27; 162(13): 1849-1855). Persistent stuttering is a fluency disorder that occurs during early childhood without obvious reasons and persists in ~1% of the adult population, predominantly in males (Yairi E and Ambrose N J, Review Epidemiology of stuttering: 21st century advances Fluency Disord. 2013 Jun; 38(2): 66-87).

Tourette syndrome (TS) is a childhood onset, neurobehavioral disorder and characterized by motor and vocal tics, and associated with a wide spectrum of behavioral and cognitive alterations. The prevalence of developing TS is four times higher in males than the female counterparts (Yairi E, Ambrose NG, Paden EP, Throneburg RN Predictive factors of persistence and recovery: pathways of childhood stuttering. J Commun Disord. 1996 Jan-Feb; 29(1): 51-77). TS is a chronic, neuro-psychiatric disorder and associated with the combination of multiple

motor tics and at least one vocal tic. Most patients suffer from psychiatric comorbidities such as attention deficit hyperactivity disorder (ADHD), obsessive compulsive disorder (OCD), self-injurious behavior, depression, and anxiety disorder. An estimated prevalence of TS is about 1% and more affected in males than females (Robertson, M.M.; Eapen, V.; Cavanna, A.E. The international prevalence, epidemiology, and clinical phenomenology of Tourette syndrome: A cross-cultural perspective. J. Psychosom. Res. 2009, 67: 475–483; Knight, T.; Steeves, T.; Day, L.; Lowerison, M.; Jette, N.; Pringsheim, T. Prevalence of tic disorders: A systematic review and meta-analysis. Pediatr. Neurol. 2012, 47: 77–90). More adversely affected patients usually display more complex tics including imitating gestures (echopraxia) and words or phrases (echolalia), and paliphenomena such as phonic blocking and repetition of own words and syllables (palilalia) (New Insights into Clinical Characteristics of Gilles de la Tourette Syndrome: Findings in 1032 Patients from a Single German Center. Sambrani T, Jakubovski E, Müller-Vahl KR Front Neurosci. 2016; 10: 415). The palilalia and vocal blocking highly affect the fluency of speech and look like the phenomenon of stuttering, leading to significant social problems (Ganos C., Müller-Vahl K., Bhatia K.P. Blocking phenomena in Gilles de la Tourette syndrome. Mov. Disord. Clin. Pract. 2015, 2: 438–439). The clinical features of TS resemble speech pathological symptoms such as stuttering and cluttering, however pathophysiology associated with both conditions are different from one another in terms of diagnosis and treatment (Dysfluency and phonic tics in Tourette syndrome: a case report. Van Borsel J, Vanryckeghem M J Commun Disord. 2000 May-Jun; 33(3): 227-239; quiz 239-40).

There is no common agreement on the pathophysiology of stuttering. Several research studies have indicated that alterations in sensory, motor, and cognitive functions, however the basis of pathophysiology has produced inconsistent or

nonreproducible results. One reliable finding reported abnormal auditory feedback systems in persons who stutter. (PWS) (Andrews G, Craig A, Feyer AM, Hoddinott S, Howie P, Neilson M; Review Stuttering: a review of research findings and theories circa 1982. J Speech Hear Disord. 1983 Aug; 48(3): 226-246).

Several neurotransmitter systems have been indicated to be associated with the pathogenesis of TS including the dopaminergic, serotonergic, glutamatergic, gamma-amino butyric acid-(GABA)ergic, histaminergic, and endocannabinoid systems (Martino, D. and Leckman, J.F. *Tourette Syndrome*. Oxford University Press, New York; 2013). The multiple evidences, however, supports a "dopaminergic hypothesis" in TS with an increased signal transduction in brain. This hypothesis is supported by the effects of dopamine receptor blocking drugs (antipsychotics) on tics (Roessner, V., Plessen, K.J., Rothenberger, A., Ludolph, A.G., Rizzo, R., Skov, L., Strand, G., Stern, J.S., Termine, C., and Hoekstra, P.J. European clinical guidelines for Tourette syndrome and other tic disorders. Part II: Pharmacological treatment. Eur. Child. Adolesc. Psychiatry. 2011; 20(4): 173–196), other findings include alterations in both presynaptic dopamine transporters (DAT) and postsynaptic dopamine D2 receptors (DRD2) in striatal and extra-striatal regions based on the detection of increased presynaptic dopamine uptake sites in both the striatum and the frontal cortex (Singer, H.S., Hahn, I.H., and Moran, T.H. Abnormal dopamine uptake sites in postmortem striatum from patients with Tourette's syndrome. Ann. Neurol. 1991; 30(4): 558–562; Minzer, K., Lee, O., Hong, J.J., and Singer, H.S. Increased prefrontal D2 protein in Tourette syndrome: a postmortem analysis of frontal cortex and striatum. J. Neurol. Sci. 2004; 219(1-2): 55–61). Several studies have revealed that alterations in dopaminergic system with increased striatal DAT binding as well as dopamine transporter binding in Gilles de la Tourette syndrome using a [123I]FP-CIT/SPECT study (Serra-Mestres,

J., Ring, H.A., Costa, D.C., Gacinovic, S., Walker, Z., Lees, A.J., Robertson, M.M., and Trimble, M.R. Dopamine transporter binding in Gilles de la Tourette syndrome: A [^{123}I]FP-CIT/SPECT study. Acta Psychiatr. Scand. 2004; 109(2): 140–146).

One study showed, based on positron emission tomography (PET) scans that a dysregulation of the dopamine system and increased dopaminergic activity is persistent in developmental stuttering. (Wu JC, Maguire G, Riley G, Lee A, Keator D, Tang C, Fallon J, Najafi A. Increased dopamine activity associated with stuttering. Neuroreport. 1997 Feb 10; 8(3): 767-770). Further, an additional study supports the theory that the hyperdopaminergic system may be involved in developmental shuttering wherein levodopa, is converted into dopamine, worsening speech fluency (Anderson JM, Hughes JD, Rothi LJ, Crucian GP, Heilman KM. Developmental stuttering and Parkinson's disease: the effects of levodopa treatment. J Neurol Neurosurg Psychiatry. 1999 Jun; 66(6): 776-778). Further in support of this notion, dopamine antagonists, such as haloperidol, risperidone or olanzapine, typically improve speech fluency (Lavid N, Franklin DL, Maguire GA Management of child and adolescent stuttering with olanzapine: three case reports. Ann Clin Psychiatry. 1999 Dec; 11(4): 233-236; Maguire GA, Yu BP, Franklin DL, Riley GD Review alleviating stuttering with pharmacological interventions. Expert Opin Pharmacother. 2004 Jul; 5(7): 1565-1571). However, the use of antipsychotics drugs for the treatment of stuttering is currently under discussion because of unwanted adverse side effects (Bothe AK, Franic DM, Ingham RJ, Davidow JH. Pharmacological approaches to stuttering treatment: reply to Meline and Harn (2008) Am J Speech Lang Pathol. 2008, 17(1): 98–101; Boyd A, Dworzynski K, Howell P. Review Pharmacological agents for developmental stuttering in children and adolescents: a systematic review. J Clin Psychopharmacol. 2011 Dec; 31(6): 740-744; Maguire GA, Yu BP, Franklin DL, Riley GD. Alleviating stuttering with

pharmacological interventions. Expert Opin Pharmacother. 2004 Jul; 5(7): 1565-1571). The stuttering-like dysfluencies also involve both increased and decreased dopamine levels (Goberman AM, Blomgren M. Parkinsonian speech disfluencies: effects of L-dopa-related fluctuations. J Fluency Disord. 2003 Spring; 28(1): 55-70).

Atypical antipsychotics such as risperidone, ziprasidone, quetiapine, clozapine, tiapride, sulpiride, and aripiprazole drugs are known to reduce dopaminergic signaling as well as far less likely to cause extrapyramidal side effects. Several clinical cases have shown that risperidone, and aripiprazole seem to be the most robust evidence-based options for the treatment of stammering. Where as quetiapine may be a promising therapy. However, ziprasidone and olanzapine are also effective, but the evidence is lacking. In terms of tic symptom score, compared with placebo, haloperidol, risperidone, aripiprazole, quetiapine, olanzapine, and ziprasidone can significantly improve tic symptom score (Chunsong Yang, Zilong Hao, Ling-Li Zhang, Cai-Rong Zhu, Ping Zhu, Qin Guo, Comparative Efficacy and Safety of Antipsychotic Drugs for Tic Disorders: A Systematic Review and Bayesian Network Meta-Analysis, Pharmacopsychiatry 2019; 52(1): 7–15).

The most common adverse events of haloperidol were drowsiness, extrapyramidal reactions, and dry mouth. The most common adverse events of tiapride and aripiprazole were dizziness, nausea, and dry mouth. Where as, risperidone also induce adverse events such as drowsiness and appetite (Chunsong Yang, Zilong Hao, Ling-Li Zhang, Cai-Rong Zhu, Ping Zhu, Qin Guo, Comparative Efficacy and Safety of Antipsychotic Drugs for Tic Disorders: A Systematic Review and Bayesian Network Meta-Analysis, Pharmacopsychiatry 2019; 52(1): 7–15).

The traditional treatment includes behavioral therapy and antipsychotic medication, which are known to induce significant side effects and with limited effectiveness in a substantial number of patients with TS (European clinical

guidelines for Tourette syndrome and other tic disorders. Part III: behavioural and psychosocial interventions. Verdellen C, van de Griendt J, Hartmann A, Murphy T, ESSTS Guidelines Group. Eur Child Adolesc Psychiatry. 2011 Apr; 20(4): 197-207). There is an urgent need for treating stammering with new and more effective treatment with fewer side effects.

The central endocannabinoid system (ECS) has been proposed as an alternative mechanism of drug action (Müller-Vahl, K.R.; Kolbe, H.; Schneider, U.; Emrich, H.M. Cannabinoids: Possible role in patho-physiology and therapy of Gilles de la Tourette syndrome. Acta Psychiatr. Scand. 1998, 98(6): 502–506). Accordingly, cannabis-based medicine (CBM) such as dronabinol (delta-9-tetrahydrocannabinol, THC) and nabiximols which contains THC and cannabidiol (CBD) at a 1:1 ratio—have been suggested as new treatment strategies for patients with TS. A recent case study indicates that with a daily high dosage of delta-9-tetrahydrocannabinol (10 mg) combined with cannabidiol (CBD) (20 mg), the patient showed a rapid and highly significant improvement in the Yale Global Tic Severity Scale (Pichler EM, Kawohl W, Seifritz E, Roser P. Pure delta-9-tetrahydrocannabinol and its combination with cannabidiol in treatment-resistant Tourette syndrome: A case report. Int J Psychiatry Med. 2018 Jul 30:91217418791455). In few clinical study cases in children with age between 16 and 19 have reported that very high doses of synthetic THC or cannabis found to result in be a significant improvement in symptoms such as vocal blocking tics as well as of comorbid conditions (Ewgeni Jakubovski and Kirsten Müller-Vahl. Speechlessness in Gilles de la Tourette Syndrome: Cannabis-Based Medicines Improve Severe Vocal Blocking Tics in Two Patients Int. J. Mol. Sci. 2017, 18(8): 1739; doi:10.3390/ijms18081739). However, the high doses of cannabis are associated with side effects.

SUMMARY

This invention provides compositions and methods for treating patients suffering from stammering, stuttering or Tourette syndrome which includes administering to such a patient THC in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient and/or CBD in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient.

In preferred embodiments, THC can be organic or synthetic and combined with atypical antipsychotic drugs such as risperidone, tiapride, sulpiride, and aripiprazole can be used with THC and/or CBD.

DESCRIPTION

Cannabis compounds can be synthetic (chemically synthesized) or extracted from cannabis plants such as sativa, indica, or hemp or hybrid strains of sativa and indica. A preferred source of tetrahydrocannabinol (THC) is so-called organic THC, which is extracted from cannabis and contains minor amounts of other cannabinoids such as CBD.

The preferred oral dose range comprising the formulation is set out in Table 1:

Table 1

Active ingredient	**Dose range per kg of body weight**
THC	0.2 µg/kg to about 0.035 mg/kg
CBD	0.2 µg/kg to about 0.035 mg/kg

Table 2

Conversion of dose for a 70-kg human:

Active ingredient	**Dose range per 70 kg of body weight**
THC	1.4 µg to about 2.5 mg
CBD	1.4 µg to about 2.5 mg

The preferred oral dose is in the range of 1 ml of an oral suspension, for a 70-Kg human, twice a day, thrice a day or four times a day depending on the severity of the symptoms comprising of a cannabis compound with up to 2.5 mg of THC, and up to 2.5 mg CBD.

The combination of lower dose of THC and CBD, compounds unexpectedly lead to a lower incidence of stammering and symptoms associated with TS.

Suitable pharmaceutically acceptable cannabis compounds include cannabis extract, which includes phytocannabinoids such as tetrahydrocannabinol "THC" (9-tetrahydrocannabinol (delta-9 THC), 8-tetrahydrocannabinol (delta-8 THC) and 9-THC acid), cannabidiol (CBD), other phytocannabinoids such as cannabinol (CBN), cannabichromene (CBC), cannabigerol (CBG) among others, terpenoids, and flavonoids. Standardized cannabis extract (SCE) consists of mostly THC, CBD, and CBN. Organic THC consists of solvent extracted THC from cannabis with lesser or trace amounts of other cannabinoids and terpenoids. Synthetic or pure THC, which is free of CBD and other compounds, is a preferred cannabis compound.

THC and CBD can be extracted from a cannabis indica dominant strain using, for example, high pressure and carbon dioxide or ethanol as a solvent in a 1500-20L

subcritical/supercritical CO_2 system made by Apeks Supercritical, 14381 Blamer Rd., Johnstown, Ohio, 43031.

Example 1

The following is a list of ingredients for making 30 ml of the formulation:

I. THC: 0.25%
II. CBD: 0.25 %
III. Honey (organic): 20% ml
IV. Vitamin-E-TPGS: 2.5%
V. Rutin: 0.05%
VI. Coconut oil (organic): 0.5 %
VII. USP Water: 80%
VIII. Ascorbic acid 1%
IX. Organic flavor: 0.05%
X. Beta-cyclodextrin: 0.5%

- Weigh 75 mg of each compound THC and CBD and dissolve in 150 mg of coconut oil using a mechanical stirrer for 6 minutes. To this add 150 mg of beta cyclodextrin and 0.750g of Vitamin-E-TPGS and mix with a mechanical stirrer for 6 minutes. Label this solution as Solution A.
- In a separate beaker, weigh 0.3 g of ascorbic acid and add 24 ml of USP grade water and 6 ml honey. Stir this mixture using a mechanical stirrer for 10 minutes. Label this as Solution B.
- To Solution B, add 1.6 mg of Rutin and mechanically stir for 7 minutes.
- Filter Solution B through a 0.2-micron filter using a vacuum filtration unit.

- Mix Solution A and the Filtered Solution B together and mechanically stir for 15 minutes.
- The final solution is stored in a bottle away from direct sunlight at room temperature.

The cannabis or hemp plant in its natural form contains THCA and CBDA. The resin called shatter is extracted from the cannabis/hemp flower using any of a variety of methods including CO_2 extraction as described herein. Shatter is produced using a three-step process: kief separation, extraction, and winterization. Cannabis flower is introduced into a steel tumbler over a mesh sieve with dry ice. Flower is frozen and broken while tumbled with dry ice chunks allowing fine THCA bearing particles (kief) to fall through the sieve. THCA is then extracted from kief using supercritical extraction. A solvent such as CO_2 and kief are introduced into a chamber. That sealed chamber is pressurized to approximately 2800 psi and heated to 53°C. Supercritical CO_2 is then allowed to flow out of the pressurized chamber into a vial at room temperature and pressure (while more CO_2 is introduced to maintain pressure in the chamber). As the CO_2 vaporizes in the collector vial, it deposits shatter. In the third, optional step, called winterization, the CO_2 oil is dissolved in ethanol (3/4 ounce shatter dissolved in 400 ml ethanol). This mixture is then poured through a filter (such as a coffee filter) frozen for 48 hours, then warmed, filtered again, and then spun with heat to evaporate off the ethanol. The remaining resin contains a combination of THCA, CBDA, and other cannabis compounds. The resin is heated for 60 minutes at 240°F. An HPLC test is run to determine the amount of THC and CBD and THCA and CBDA present in the resin.

75 mg of the resin containing 99% THC and CBD (as determined by HPLC) is dissolved in 150 mg of organic coconut oil. The dissolved resin is transferred and

mixed with the solution of -honey-ascorbic acid-rutin-vitamin-E-TPGS. The solution is filtered and sterilized using a 0.2-micron PES Nalgene filtration unit under constant pressure in a sterilized environment. The filtered 30 ml solution is transferred to and stored in an amber glass bottle that is autoclaved in an aseptic condition.

Example 2: A TS patient exhibiting multiple motor and vocal tics an hour is given 1 ml of the formulation of Example 1, in the morning on an empty stomach, prior to breakfast, and 1 ml prior to dinner in the evening. The patient after three days of therapy exhibits reduced motor and vocal tics with no side effects commonly associated with cannabis.

Example 3: A stuttering patient exhibiting continuous conversational stuttering is given 1 ml of the formulation of Example 1, in the morning on an empty stomach, prior to breakfast, and 1 ml prior to dinner in the evening. The patient exhibits reduced vocal stuttering.

Example 4: A patient exhibiting conversational stuttering during stress is given 1 ml of the formulation of Example 1 via a spray prior to the onset of stress. The patient exhibits reduced vocal stuttering and manages to have a near stuttering free conversation.

Example 5: A patient with advance stage TS exhibiting moderate to severe anxiety, sleep disorder and/or multiple motor tics and several vocal (phonic) conversational stuttering is given 1 ml of the formulation of Example 1 three times a day, morning afternoon and evening, prior to meals. The patient exhibits reduced anxiety and agitation and caregiver distress.

Example 6: The formulation of Example 1, without the THC component, is administered three times a day prior to meals to a moderate stage attention deficit

hyperactivity disorder (ADHD), obsessive compulsive disorder (OCD), self-injurious behavior, depression, and anxiety disorder with a decrease in all symptoms.

Example 7: A male patient displaying stammering and taking standard atypical anti-psychotic drug treatment. The said patient is administered the formulation of Example 1 without the CBD component which over three days leads to a decrease in the anti-psychotic medication and associated side effects of the atypical anti-psychotic drug medication.

Example 8: A patient displaying stammering and taking standard atypical anti-psychotic drug is administered the formulation of Example 1 without the THC component. Over three days the patient exhibits a decrease in the atypical anti-psychotic drug medication and associated side effects of the anti-psychotic drug medication.

Example 9: A male patient age 17 displaying stammering and on standard atypical anti-psychotic drug is administered the formulation of Example 1 without THC. The patient, after 5 days of treatment, exhibits a decrease in the atypical anti-psychotic medication and associated side effects of the anti-psychotic drug medication.

Example 10: A male patient age 14 displays stammering as measured on the Speech Efficiency Score (SES) scale of 11. The patient is administered the formulation of Example 1 without the THC component. After a period of two weeks the patient exhibits an SES score of 6.

CLAIMS

Claim 1. Composition for treating a patient suffering from stammering, stuttering or Tourette syndrome comprising THC in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient and CBD in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient.

Claim 2. Composition for treating a patient suffering from stammering, stuttering, and Tourette syndrome comprising THC in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient.

Claim 3. Composition for treating a patient suffering from stammering, stuttering, and Tourette syndrome comprising CBD in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient.

Claim 4. Composition of claim 1 or 2 wherein the THC is organic or synthetic.

Claim 5. Composition claims 1 or 2 which includes an atypical antipsychotic drug selected from the group consisting of risperidone, clozapine, olanzapine, ziprasidone, tiapride, sulpiride, and aripiprazole.

Claim 6. Composition claim 3 which includes an atypical antipsychotic drug selected from the group consisting of risperidone, clozapine, olanzapine, ziprasidone, tiapride, sulpiride, and aripiprazole.

Claim 7. Composition of claims 1, 2 or 3 in the form of oral drops or an oral spray.

Claim 8. Method for treating a patient suffering from stammering, stuttering or Tourette syndrome comprising administering to said patient a composition comprising THC in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient and CBD in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient.

Claim 9. Method for treating a patient suffering from stammering, stuttering or Tourette syndrome comprising administering to said patient a composition comprising THC in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient.

Claim 10. Method for treating a patient suffering from stammering, stuttering or Tourette syndrome comprising administering to said patient a composition comprising CBD in the range of about 0.2 µg/kg to about 0.035 mg/kg of a patient.

Claim 11. Method of claim 8 or 9 wherein the THC is organic or synthetic.

Claim 12. Method claims 8 or 9 which includes an atypical antipsychotic drug selected from the group consisting of risperidone, clozapine, olanzapine, ziprasidone, tiapride, sulpiride, and aripiprazole.

Claim 13. Composition claim 10 which includes an atypical antipsychotic drug selected from the group consisting of risperidone, clozapine, olanzapine, ziprasidone, tiapride, sulpiride, and aripiprazole.

Claim 14. Method of claims 8, 9 or 10 wherein said composition is administered in the form of oral drops or an oral spray.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/34602

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 31/01; A61K 31/015; A61K 31/045 (2020.01)

CPC - A61K 31/01; A61K 31/015; A61K 31/045; A61K 31/05

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)
See Search History document

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	Kanaan et al. Significant Tic Reduction in An Otherwise Treatment-Resistant Patient with Gilles de la Tourette Syndrome Following Treatment with Nabiximols. 26 April 2017 [Retrieved 09 August 2020] Retrieved from Internet URL: < https://pubmed.ncbi.nlm.nih.gov/28445405/ >	1-4, 7-11, and 14 ---------- 5-6, 12-13
Y	US 2016/0271141 A1 (Psyadon Pharmaceuticals INC) 22 September 2016 (22.09.2016) Abstract; Para [0004]; [0080]; [0091]	5-6, 12-13
A	US 2016/0000815 A1 (Gosforth Centre Holdings PTY LTD) 07 January 2016 (07.01.2016) entire document	1-14
A	US 2018/0064055 A1 (Biotech Institute LLC) 08 March 2018 (08.03.2018) entire document	1-14

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
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"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)
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Date of the actual completion of the international search	Date of mailing of the international search report
09 August 2020	27 AUG 2020
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300