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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
6 July 2017 (06.07.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/116190 A1

(51) **International Patent Classification**:
A61K 9/48 (2006.01) *A61K 47/14* (2006.01)
A61K 47/10 (2006.01) *A61K 31/568* (2006.01)

(21) **International Application Number**:
PCT/KR2016/015533

(22) **International Filing Date**:
29 December 2016 (29.12.2016)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
10-2015-0190815
31 December 2015 (31.12.2015) KR

(71) **Applicants**: **YUYU PHARMA, INC.** [KR/KR]; 94, Bio valley 1-ro, Jecheon-si, Chungcheongbuk-do 27159 (KR). **AJOU UNIVERSITY INDUSTRY-ACADEMIC CO-OPERATION FOUNDATION** [KR/KR]; 206, World cup-ro, Yeongtong-gu, Suwon-si, Gyeonggi-do 16499 (KR).

(72) **Inventors**: **BAIK, Taegon**; 503, 21-39 Jingwan 1-ro, Eunpyeong-gu, Seoul 03311 (KR). **KIM, Seyeon**; 831-1504, 26, Yeongtong-ro 290beon-gil, Yeongtong-gu, Suwon-si, Gyeonggi-do 16698 (KR). **AHN, Kyeongjin**; (WorldMerdian), #101, 20, Banpodaero 26gil, Seochogu, Seoul 06648 (KR). **KIM, Ju-hee**; 915-1402, 27, Bongyeong-ro 1517beon-gil, Yeongtong-gu, Suwon-si, Gyeonggi-do 16700 (KR). **PARK, Young-joon**; 504-907, 111, Byeoryang-ro, Gwacheon-si, Gyeonggi-do 13836 (KR).

(74) **Agent**: **SHIN, Yoon Suk**; Lee International IP & Law Group, 14th Fl., Poongsan Bldg., 23 Chungjeongro, Seodaemun-gu, Seoul 03737 (KR).

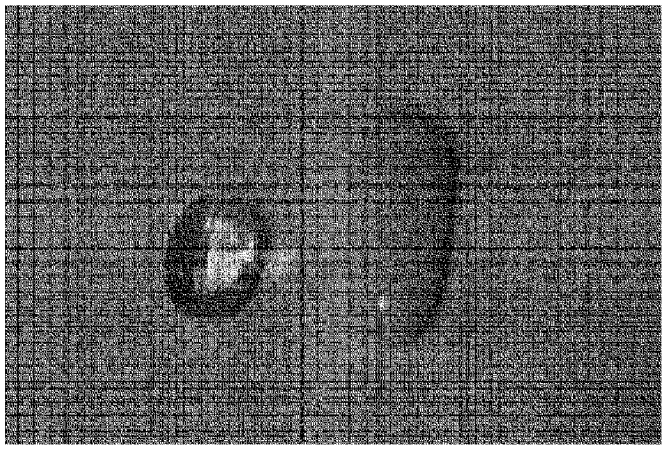
(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, 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, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, 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))*

(54) **Title**: PHARMACEUTICAL COMPOSITION COMPRISING DUTASTERIDE AND PROPYLENE GLYCOL MONOLAURATE AND PREPARATION METHOD OF THE SAME



(57) **Abstract**: The present invention relates to a pharmaceutical composition comprising dutasteride and propylene glycol monolaurate, which improves the stability of dutasteride, which is a poorly soluble drug as a 5-alpha reductase inhibitor, and a process for its preparation. More particularly, the present invention also relates to a capsule formulation which is smaller in size than a commercial dutasteride capsule formulation (AVODART®), but has the equivalent dissolution rate by preparing a pharmaceutical composition comprising propylene glycol monolaurate and dutasteride, which can improve the stability of the dutasteride. A dutasteride formulation having enhanced patient's compliance and improved stability and a method for producing the same are provided.

WO 2017/116190 A1

Description

Title of Invention: PHARMACEUTICAL COMPOSITION COMPRISING DUTASTERIDE AND PROPYLENE GLYCOL MONOLAURATE AND PREPARATION METHOD OF THE SAME

Technical Field

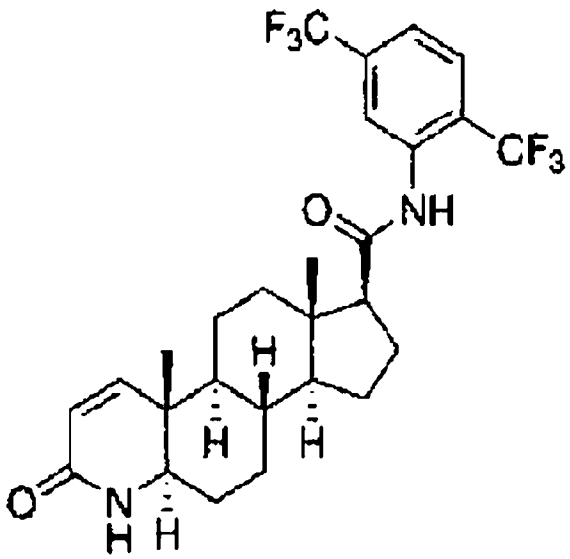
[1] The present disclosure relates to a pharmaceutical composition comprising dutasteride, a capsule formulation comprising the same, and a preparation method of the same. More particularly, the present invention further relates to a pharmaceutical formulation reducing the size of the capsule with improved stability.

Background Art

[2] US Patent No. 5,565,467 discloses that dutasteride (chemical name: 17β-N-(2,5-bis(trifluoromethyl))phenylcarbamoyl-4-aza-5α-androst-1-en-3-one) of the following Formula (I), a 5-alpha reductase inhibitor, is capable of being used in treating benign prostate hyperplasia, prostate cancer and male pattern alopecia (androgenetic alopecia).

[3] <Formula (I)>

[4]



[5] Dutasteride is commercially available as AVODART® soft gelatin capsule (size of 6 oblong) which contains 0.5 mg of dutasteride dissolved in 349.5 mg of a mixture of mono- and di-glyceride of caprylic/capric acid and butylated hydroxy toluene (BHT).

[6] However, in order to fill the active ingredient, dutasteride into the soft gelatin capsule, a large amount of oils and surfactants are required to be used, leading to an increase in the size of the capsule. The large-sized capsule may cause low patient

compliance due to patient's inability or unwillingness to swallow the large-sized formulations. In particular, considering that the great majority of benign prostate hyperplasia patients is elderly patients and long-term use of dutasteride is required for the treatment, the large size of the dutasteride capsule leads to disadvantages in that taking such large capsule is very inconvenient for elderly patients and thus patient compliance is low.

[7] Korean Patent No. 10-1055412 discloses a method for preparing a tablet of dutasteride by using a self-emulsifying drug delivery system. However, in order to prepare tablets with improved dissolution characteristics of poorly water-soluble drug, dutasteride, additional excipients such as surfactants and absorbents are needed and the preparation method is somehow complicated as the two-times coating is required. Further, a large amount of absorbents are required, leading to an increase in the size of the capsule which is likely to cause the problem in patient compliance.

[8] Korean Patent Publication No. 10-2013-0086551 discloses a method of improving solubility and bioavailability of dutasteride by using a self-emulsifying drug delivery system. However, a large amount of surfactant (equal to or more than 20% of total composition) is used in the self-emulsifying drug delivery system, thereby causing low stability (decrease in moisture and increase in hardness of gelatin used as a capsule base and the subsequent delayed disintegration and low dissolution rate).

[9] The present inventors of the present invention have conducted a research on formulation of dutasteride to develop a pharmaceutical composition having smaller content in the capsule than that of AVODART® capsule, and having excellent stability even though the amount of the capsule content to be filled is low. They discovered that propylene glycol monolaurate is used as an excellent solubilizer that dissolves dutasteride, thereby causing decrease in the size of the dutasteride capsule, while ensuring an equivalent dissolution rate as that of AVODART®, as well as an improved stability.

Disclosure of Invention

Technical Problem

[10] The present disclosure provides a pharmaceutical composition comprising dutasteride which is characterized by improved solubility of dutasteride, the reduction in the capsule size, and improved stability, and a preparation method of the same.

[11] The technical problem of the present disclosure are not limited to the technical problem described above, and other technical problems that are not described will be clear to those skilled in the art from the description provided below.

Solution to Problem

[12] In one aspect, the present disclosure relates to a pharmaceutical composition

comprising dutasteride and propylene glycol monolaurate.

[13] According to one embodiment of the present pharmaceutical composition, the content of dutasteride is greater than or equal to 0.1% by weight and less than or equal to 3.0% by weight, and the content of propylene glycol monolaurate is greater than or equal to 97.0% by weight and less than or equal to 99.9% by weight based on the total of the pharmaceutical composition.

[14] According to another embodiment of the present pharmaceutical composition, the pharmaceutical composition further comprises pharmaceutically acceptable excipients.

[15] In another aspect, the present disclosure relates to a capsule formulation comprising the pharmaceutical composition. The capsule formulation is soft or hard capsule fomulation.

[16] According to one embodiment of the present capsule formulation, the pharmaceutical composition is filled in a liquid phase.

[17] In another aspect, the present disclosure relates to a method of preparing the capsule formulation, comprising dissolving dutasteride in propylene glycol monolaurate to obtain a clear solution of dutasteride; and filling the obtained clear solution in a capsule.

[18] Other embodiments of the present disclosure are included in the detailed description and the drawings.

Advantageous Effects of Invention

[19] The present pharmaceutical composition comprising dutasteride uses propylene glycol monolaurate, which has high solubility and stability to dutasteride, as a solubilizer, thereby solving the problem of the poor solubility of dutasteride, reducing the size of the dutasteride capsule formulation, improving patient compliance, and increasing stability of dutasteride.

[20] Effects of the present disclosure are not limited to the effects illustrated above, and more various effects are included in the present specification.

Brief Description of Drawings

[21] FIG. 1 shows the comparison of the appearance of a capsule prepared according to one embodiment of the present disclosure and a commercially-available AVODART® capsule.

[22] FIG. 2 shows a graph of dissolution rate comparison tests of comparative examples and an example of the present disclosure.

Mode for the Invention

[23] The present disclosure provides a pharmaceutical composition comprising dutasteride and propylene glycol monolaurate. That is, the present invention relates to a pharmaceutical composition in which the solubility of the poorly-soluble drug, du-

tasteride is improved, thereby reducing the size of the final oral capsule formulation, and hence improving the patient's compliance, while ensuring capsule stability to have an equivalent dissolution rate as that of an existing product; a method of manufacturing the pharmaceutical composition; and an oral capsule formulation filled with the pharmaceutical composition. The capsule formulation according to one embodiment of the present disclosure is expected to exhibit characteristics of rapid absorption and excellent stability upon oral administration.

[24] In the pharmaceutical composition comprising dutasteride according to one embodiment of the present disclosure, propylene glycol monolaurate is used as a capsule filling oil component because propylene glycol monolaurate exhibits excellent solubility improvement effects of an active ingredient, dutasteride, and has characteristics as a pharmaceutically acceptable excipient capable of ensuring the stability of dutasteride when dissolved. One embodiment of the present disclosure may further use an antioxidant that may enhance stabilization of propylene glycol monolaurate, and the like.

[25] Hereinafter, detailed composition of the pharmaceutical composition according to one embodiment of the present disclosure and a method of manufacturing the pharmaceutical composition will be described with reference to embodiments and comparative examples.

[26] Test Example 1 is a test result comparing the solubility of dutasteride depending on the types of oil. As identified in Table 5 of Test Example 1, dutasteride, an active ingredient of the present disclosure, is not favorably soluble in oil such as glycerol tricaprylate, glycerol tricaprylate/caprate, glycerol tricaprylate/caprate/linoleate, propylene glycol dicaprylocaprate, propylene glycol dicaprate, and propylene glycol dicaprylate. However, the solubility of dutasteride is much higher in propylene glycol monolaurate than that in other oils.

[27] In Test Example 2, in order to identify the stability of dutasteride in oil, the oil and dutasteride are mixed at a ratio of about 10 to 1, and then a stability test is carried out under an accelerated and stress condition, and a percentage of generated unknown degradation products with respect to the active ingredient is calculated to confirm whether degradation products are generated or not.

[28] As shown in the following Table 6, the stability of dutasteride in oil is identified as follows: a relatively large amount of degradation products is generated in mono- and di-glyceride of caprylic/capric acid used in an existing AVODART® soft capsule under both accelerated and stress conditions. However, degradation products were not generated in propylene glycol monolaurate even when stored under the accelerated condition for 4 weeks. In addition, even when stored under the stress condition for 4 weeks, a relatively small amount of degradation products is generated, as compared to

that in mono- and di-glyceride of caprylic/capric acid.

[29] Based on the solubility and stability tests, it was identified that propylene glycol monolaurate is capable of enhancing solubility and stability of dutasteride in the pharmaceutical composition according to one embodiment of the present disclosure.

[30] In addition, the composition according to one embodiment of the present disclosure may use a pharmaceutically acceptable excipient for oral administration, for example, an antioxidant, an colorant, and a preservative, within the scope that does not obscure the purpose of the present disclosure. Example of the antioxidant may include butylated hydroxy toluene (BHT), butylated hydroxy anisole (BHA) and the like.

[31] In addition, embodiments of the present disclosure also provide a method of manufacturing a pharmaceutical composition comprising dutasteride that comprises a step of dissolving dutasteride in propylene glycol monolaurate. In the aforementioned manufacturing method, dutasteride and propylene glycol monolaurate may be mixed so that dutasteride is homogeneously dissolved in propylene glycol monolaurate in a liquid phase.

[32] In addition, embodiments of the present disclosure provide an oral capsule formulation filled with the pharmaceutical composition comprising dutasteride. The pharmaceutical composition may be manufactured as a soft capsule formulation using a capsule base such as a generally used gelatin (or succinylated gelatin) and a plasticizer (e.g., glycerin, citric acid, sorbitol solution, glycine and propylene glycol) and using a conventional rotary type automatic filler.

[33] In addition, the pharmaceutical composition may be filled into a hard capsule, using a hard capsule manufacturing apparatus for liquid filling. Examples of bases used in the hard capsule may include gelatin/hydroxypropylmethylcellulose and a plasticizer (e.g., glycerin, citric acid, sorbitol solution, glycine and propylene glycol).

[34] The amount of the pharmaceutical composition being filled in the oral capsule formulation can be 92 mg to 185 mg, preferably 100 mg to 150 mg, more preferably 110 mg. The oral capsule formulation of the present disclosure can be prepared in size 2 oval (minims: 1.5-1.8, cc: 0.092-0.111), size 3 oval (minims: 2.4-3.0, cc: 0.148-0.185), size 3 oblong (minims: 2.3-3.0, cc: 0.142-0.185), size 4 oblong (minims: 3.0-4.0, cc: 0.185-0.246) and the like.

[35] The oral capsule formulation filled with the pharmaceutical composition comprising dutasteride according to one embodiment of the present disclosure has a relatively small size and an equivalent dissolution rate as compared to those of AVODART®, a commercial formulation, through the use of propylene glycol monolaurate which may enhance solubility and stability of dutasteride. When referring to Figure 1, the size of the oral capsule formulation according to one embodiment of the present disclosure is 2 oval (see the left picture in Figure 1), and is smaller compared to size 6 oblong of

AVODART® (minims: 5.0-6.0, cc: 0.308-0.370, see the right picture in Figure 1). Further, when referring to Figure 2, the dissolution rate of the oral capsule formulation according to one embodiment of the present disclosure (see the square shape in Figure 2) is equivalent as compared to those of AVODART® (see the round shape in Figure 2).

[36] Hereinafter, embodiments of the present disclosure will be described in more detail. The present disclosure may, however, be embodied in many different forms and should not be construed as being limited to the embodiments set forth herein.

[37] [Example 1]

[38] To a 3 L preparation container equipped with a stirrer, 1,094.9 g of propylene glycol monolaurate was added, and while stirring, 5 g of dutasteride was slowly added thereto and completely dissolved. 0.1 g of butylated hydroxy toluene was added thereto, and the resultant mixture was stirred to manufacture a pharmaceutical composition comprising dutasteride. Separately, to prepare a soft capsule shell, a shell-forming agent was prepared using gelatin, a plasticizer and the like according to the composition shown in the following Table 1. After filling a size 2 oval soft capsule with 110 mg of the prepared solubilized composition using a rotary type automatic filler to a total weight of 230 mg, drying and sorting processes were carried out to manufacture an oral soft capsule formulation.

[39] [Table 1]

Composition of oral soft capsule shell

Content	Weight (g)
Gelatin	833.2
Concentrated glycerin	256.7
D-sorbitol solution	110.1
Total	1200.0

[40]

[41] [Example 2]

[42] To a 3 L preparation container equipped with a stirrer, 194.9 g of propylene glycol monolaurate was added, and while stirring, 5 g of dutasteride was slowly added thereto and completely dissolved. 0.1 g of butylated hydroxy toluene was added thereto, and the resultant mixture was stirred to manufacture a pharmaceutical composition comprising dutasteride. Separately, to prepare a soft capsule shell, a shell-forming agent was prepared using succinylated gelatin, a plasticizer and the like according to the composition shown in the following Table 2. After filling a size 2 oval soft capsule with 110 mg of the prepared solubilized composition using a rotary type automatic

filler to a total weight of 230 mg, drying and sorting processes were carried out to manufacture an oral soft capsule formulation.

[43] [Table 2]

Composition of oral soft capsule shell

Content	Weight (g)
Succinylated gelatin	854.0
Concentrated glycerin	242.0
D-sorbitol solution	104.0
Total	1200.0

[44]

[45] [Examples 3 to 9]

[46] To a 500 mL preparation container equipped with a stirrer, oils were added in the amounts shown in the following Table 3, and while stirring, 0.5 g of dutasteride was slowly added thereto and completely dissolved. Separately, to prepare a soft capsule shell, a shell-forming agent was prepared using succinylated gelatin, a plasticizer and the like according to the composition shown in the above Table 2. After filling the composition manufactured according to Table 3 using a rotary type automatic filler, drying and sorting processes were carried out to manufacture an oral soft capsule formulation.

[47] [Table 3]

Content (g/formulation)	Example 3	Example 4	Example 5	Example 6	Example 7	Example 8	Example 9
Dutasteride	0.5 g	0.5 g	0.5 g	0.5 g	0.5 g	0.5 g	0.5 g
Propylene glycol monolaurate	104 g	150 g	220 g	150 g	220 g	160 g	220 g
Soft capsule size	2 round	3 round	4 round	3 oval	4 oval	3 oblong	4 oblong

[48]

[49] [Examples 10 and 11]

[50] To a 500 mL preparation container equipped with a stirrer, oils were added in the amounts shown in the following Table 4, and while stirring, 0.5 g of dutasteride was

slowly added thereto and completely dissolved. Separately, to prepare a soft capsule shell, a shell-forming agent was prepared using succinylated gelatin, a plasticizer and the like according to the composition shown in the above Table 2. After filling the composition manufactured according to Table 4 using a rotary type automatic filler, drying and sorting processes were carried out to manufacture an oral soft capsule formulation.

[51] [Table 4]

Content (g/formulation)	Example 10	Example 11
Dutasteride	0.5 g	0.5 g
Propylene glycol monolaurate	49.5 g	29.5 g
Soft capsule size	2 round	2 round

[52]

[53] [Comparative Example 1] Commercially available formulation

[54] A currently commercially-available AVODART® 0.5 mg soft capsule corresponding to 0.5 mg of dutasteride was used.

[55]

[56] [Test Example 1] Evaluation of oil solubility

[57] In order to measure the solubility of dutasteride in oil, the solubility of dutasteride in glycerol tricaprylate, glycerol tricaprylate/caprate, glycerol tricaprylate/caprate/linoleate, propylene glycol dicaprylocaprate, propylene glycol dicaprate, propylene glycol dicaprylate and propylene glycol monolaurate was measured. In a 10 mL vial, a magnetic bar was placed. After 3 mL of the oil was added thereto, approximately 100 mg of dutasteride was added thereto while stirring under a room temperature (25°C) condition, and the resultant mixture was stirred at 500 rpm or higher. After stirring for 24 hours, 1 mL of the resultant mixture was taken and separated using a centrifuge, and only a supernatant was taken to quantify an amount of dutasteride dissolved in the oil using liquid chromatography. As for the solubility in each oil obtained from the test results, propylene glycol monolaurate exhibited higher solubility by 10 times or greater compared to other tested oils, as shown in Table 5.

[58] [Table 5]

Solubility of dutasteride depending on oil type

Oil	Solubility (mg/mL)
Glycerol tricaprylate	0.84
Glycerol tricaprylate/caprate	0.81
Glycerol tricaprylate/caprate /linoleate	0.22
Propylene glycol dicaprylroccaprate	0.97
Propylene glycol dicaprate	0.77
Propylene glycol dicaprylate	1.13
Propylene glycol monolaurate	10.43

[59]

[60] [Test Example 2] Test on stability of dutasteride depending on oil type

[61] In order to identify the stability of dutasteride in mono- and di-glyceride of caprylic/capric acid used as an oil phase of AVODART®, an existing commercially-available formulation, the stability of dutasteride was compared under the stress condition (50℃, 95 %RH) and the accelerated condition (40℃, 75 %RH). In the comparison test, a sample prepared by dissolving 1.0 mg of dutasteride in 10.0 mg of propylene glycol monocaprylate and stored in a transparent vial and a sample prepared by dissolving 1.0 mg of dutasteride in 10.0 mg of mono- and di-glyceride of caprylic/capric acid and stored in a transparent vial were used. A percentage of degradation products with respect to dutasteride, an active ingredient, was calculated and summarized in the following Table 6.

[62] [Table 6]

Stability results of dutasteride depending on oil type

	Stress condition(50℃, 95 %RH)				Accelerated condition(40℃, 75 %RH)
	Week 1	Week 2	Week 3	Week 4	Week 4
Propylene glycol monolaurate	None	None	None	0.32 %	None
mono- and di-glyceride of caprylic/capric acid	None	None	None	1.75 %	0.94 %

[63]

[64] As can be identified from Table 6, the stability of dutasteride in propylene glycol monolaurate was more superior compared to that in mono- and di-glyceride of caprylic/capric acid in the week 4 under the accelerated condition (40 , 75 %RH) and the stress condition (50℃, 95 %RH).

[65]

[66] [Test Example 3] Comparative dissolution test with AVODART®

[67] A dissolution evaluation was carried out on the oral soft capsule formulation filled with the composition of self-emulsifying drug delivery system manufactured in the above Example 2 and the commercially-available AVODART® 0.5 mg soft capsule of Comparative Example 1. The dissolution test was carried out in accordance with Method 2 of the dissolution test method in the Korean Pharmacopoeia 10th edition using a 0.3 % aqueous lauryl sodium sulfate solution as an eluent and a rotation speed of 50 rpm.

[68] [Table 7]

Result of dissolution evaluation

	Example 2 (%)	Comparative Example 1 (%)
5 minutes	0	0
10 minutes	25.2	19.3
15 minutes	54.3	46.3
30 minutes	74.9	68.8
45 minutes	80.6	80.6

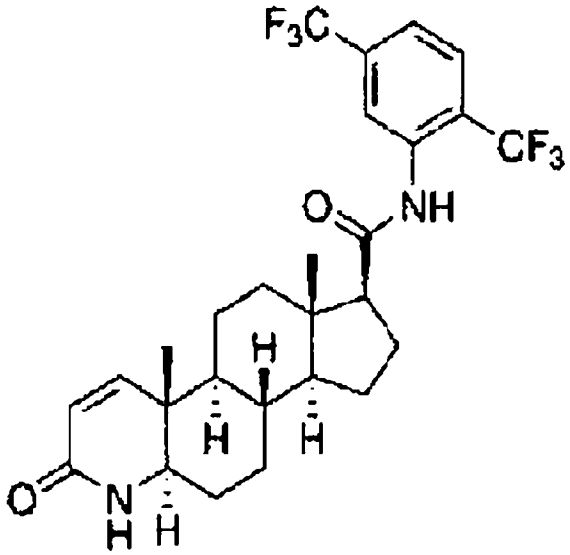
[69]

[70] As shown in the above Table 7 and FIG. 2, it was identified that the oral soft capsule formulation of Example 2 of the present disclosure had a dissolution rate similar to that of AVODART® of Comparative Example 1. Accordingly, according to one embodiment of the present disclosure, a soft capsule formulation for oral administration filled with the pharmaceutical composition comprising dutasteride that is reduced in size but has an equivalent dissolution rate as compared to those of the existing formulation has been developed.

Claims

[Claim 1] A pharmaceutical composition comprising dutasteride of the following Formula (I) and propylene glycol monolaurate:

<Formula (I)>



[Claim 2] The pharmaceutical composition of Claim 1, wherein the content of dutasteride is greater than or equal to 0.1% by weight and less than or equal to 3.0% by weight, and the content of propylene glycol monolaurate is greater than or equal to 97.0% by weight and less than or equal to 99.9% by weight based on the total of the pharmaceutical composition.

[Claim 3] The pharmaceutical composition of Claim 1, further comprising pharmaceutically acceptable excipients.

[Claim 4] An oral soft or hard capsule formulation comprising the pharmaceutical composition of any one of Claims 1 to 3.

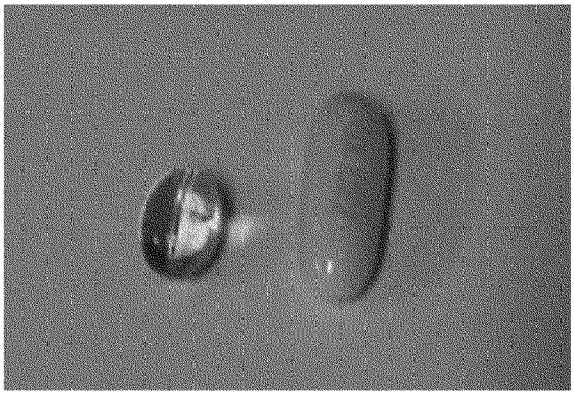
[Claim 5] The capsule formulation of Claim 4, wherein the pharmaceutical composition is filled in a liquid phase.

[Claim 6] A method of preparing the oral capsule formulation of dutasteride, comprising:

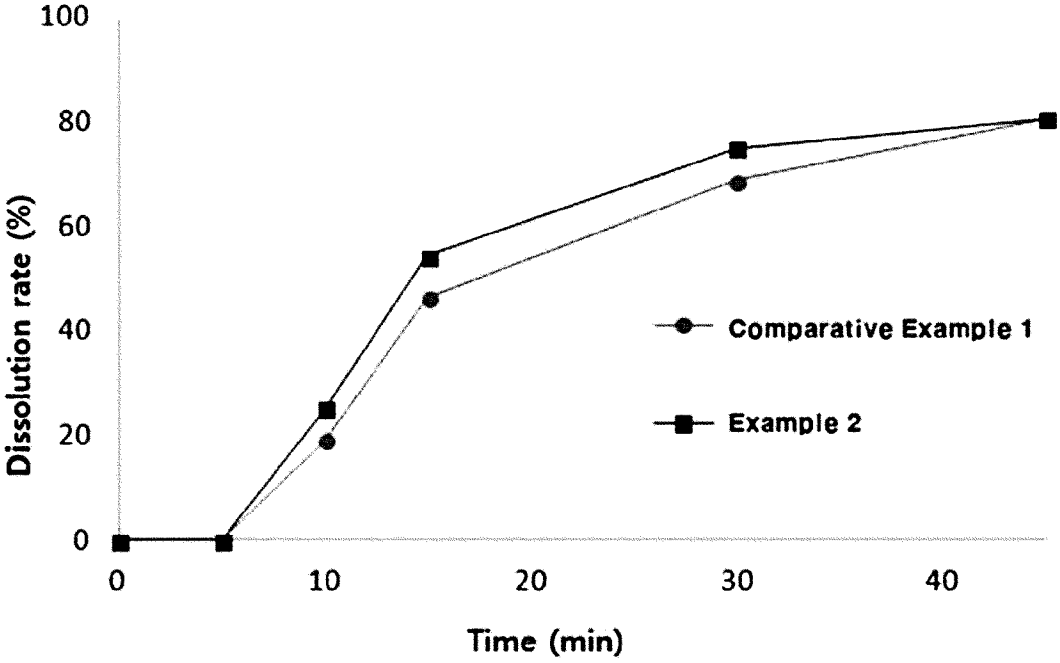
dissolving dutasteride in propylene glycol monolaurate to obtain a clear solution of dutasteride; and

filling the obtained clear solution in a capsule.

[Fig. 1]



[Fig. 2]


100
80
60
40
20
0
Dissolution rate (%)
0
10
20
30
40
Time (min)
Comparative Example 1
Example 2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2016/015533

A. CLASSIFICATION OF SUBJECT MATTER

A61K 9/48(2006.01)i, A61K 47/10(2006.01)i, A61K 47/14(2006.01)i, A61K 31/568(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)
A61K 9/48; A61K 9/20; A61K 9/107; A61K 45/00; A61K 31/473; A61K 31/568; A61K 47/38; A61K 47/26; A61K 47/10; A61K 47/14

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: dutasteride, propylene glycol monolaurate, capsule

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2012-076516 A1 (KRKA, TOVARNA ZDRAVIL, D.D., NOVO MESTO) 14 June 2012 See pages 6, 7, 13-15, 22; and claims 1, 5, 13, 14.	1-6
Y	WO 2010-092596 A1 (GENEPHARM INDIA PRIVATE LIMITED) 19 August 2010 See pages 6, 7; and claims 1, 2, 6.	1-6
A	KR 10-2013-0124414 A (CLARUS THERAPEUTICS, INC.) 13 November 2013 See the whole document.	1-6
A	JP 2014-528900 A (ANTERIOS, INC.) 30 October 2014 See the whole document.	1-6
A	JP 2007-516259 A (MEDCRYSTALFORMS, LLC.) 21 June 2007 See the whole document.	1-6
PX	KR 10-1679992 B1 (YUYU PHARMA. INC. et al.) 28 November 2016 See claims 1, 3-5.	1-6

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

☒ See patent family annex.

* 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 priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"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
"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
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
07 April 2017 (07.04.2017)	**07 April 2017 (07.04.2017)**

Name and mailing address of the ISA/KR
International Application Division
Korean Intellectual Property Office
189 Cheongsa-ro, Seo-gu, Daejeon, 35208, Republic of Korea
Facsimile No. +82-42-481-8578

Authorized officer
PARK, Jung Min
Telephone No. +82-42-481-3516

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR2016/015533

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2012-076516 A1	14/06/2012	EA 201390662 A1	29/11/2013
		EP 2468262 A1	27/06/2012
		EP 2648700 A1	16/10/2013
WO 2010-092596 A1	19/08/2010	EP 2395975 A1	21/12/2011
		EP 2395975 A4	22/05/2013
KR 10-2013-0124414 A	13/11/2013	CA 2604943 A1	26/10/2006
		CA 2604943 C	17/09/2013
		CN 101217963 A	09/07/2008
		EP 1871384 A2	02/01/2008
		EP 2979699 A1	03/02/2016
		EP 2985026 A1	17/02/2016
		JP 2008-537960 A	02/10/2008
		JP 2013-121986 A	20/06/2013
		JP 2016-074677 A	12/05/2016
		JP 5778705 B2	16/09/2015
		JP 5887044 B2	16/03/2016
		KR 10-1382725 B1	08/04/2014
		KR 10-2008-0009201 A	25/01/2008
		US 2008-0317844 A1	25/12/2008
		US 8241664 B2	14/08/2012
		WO 2006-113505 A2	26/10/2006
		WO 2006-113505 A3	17/01/2008
JP 2014-528900 A	30/10/2014	AU 2012-209339 A1	12/09/2013
		CN 103747782 A	23/04/2014
		EP 2667854 A1	04/12/2013
		JP 2016-121175 A	07/07/2016
		JP 5938838 B2	22/06/2016
		KR 10-2014-0003572 A	09/01/2014
		SG 193970 A1	29/11/2013
		US 2012-328702 A1	27/12/2012
		US 2015-196490 A1	16/07/2015
		WO 2012-103035 A1	02/08/2012
		ZA 201306391 B	30/04/2014
JP 2007-516259 A	21/06/2007	CA 2548281 A1	23/06/2005
		CA 2548281 C	12/11/2013
		EP 1727520 A2	06/12/2006
		JP 2011-256175 A	22/12/2011
		JP 2015-091773 A	14/05/2015
		US 2005-181041 A1	18/08/2005
		WO 2005-055983 A2	23/06/2005
		WO 2005-055983 A3	01/03/2007
KR 10-1679992 B1	28/11/2016	None	