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(54) **ORAL FILM PREPARATION**

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(57) **ABSTRACT**

The present invention relates to an oral film preparation obtained by spreading a solution containing a high potency drug and a film-forming polymer and then drying the solution, and a method for preparing an oral film preparation containing a high potency drug, said method comprising spreading a solution containing the high potency drug and a film-forming polymer and then drying the same, and a package obtained by (a) packaging the oral film preparation in a packaging material and, after nitrogen substitution, sealing the packaging material, and/or (b) sealing the oral film preparation together with a deoxidant in a packaging material. Provided are an oral film preparation that contains a high potency drug and has excellent content uniformity, a method for easily preparing an oral film preparation that contains a high potency drug and has excellent content uniformity, and a highly stable package that contains the oral film preparation.

FIG. 1

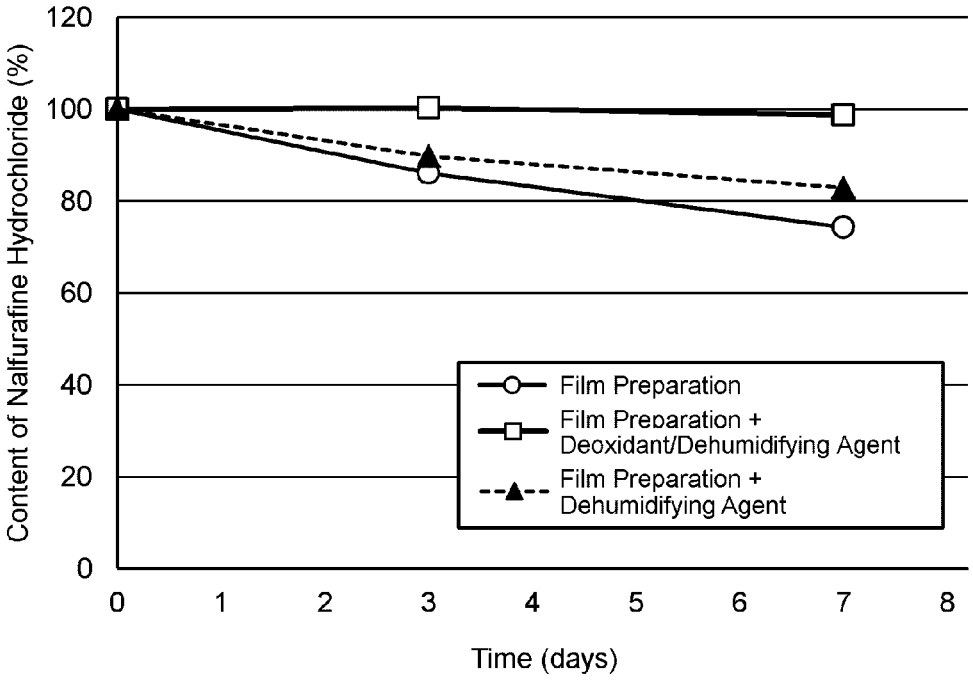

120
100
80
60
40
20
0
Content of Nalfurafine Hydrochloride (%)
0
1
2
3
4
5
6
7
8
Time (days)
Film Preparation
Film Preparation + Deoxidant/Dehumidifying Agent
Film Preparation + Dehumidifying Agent

FIG. 2

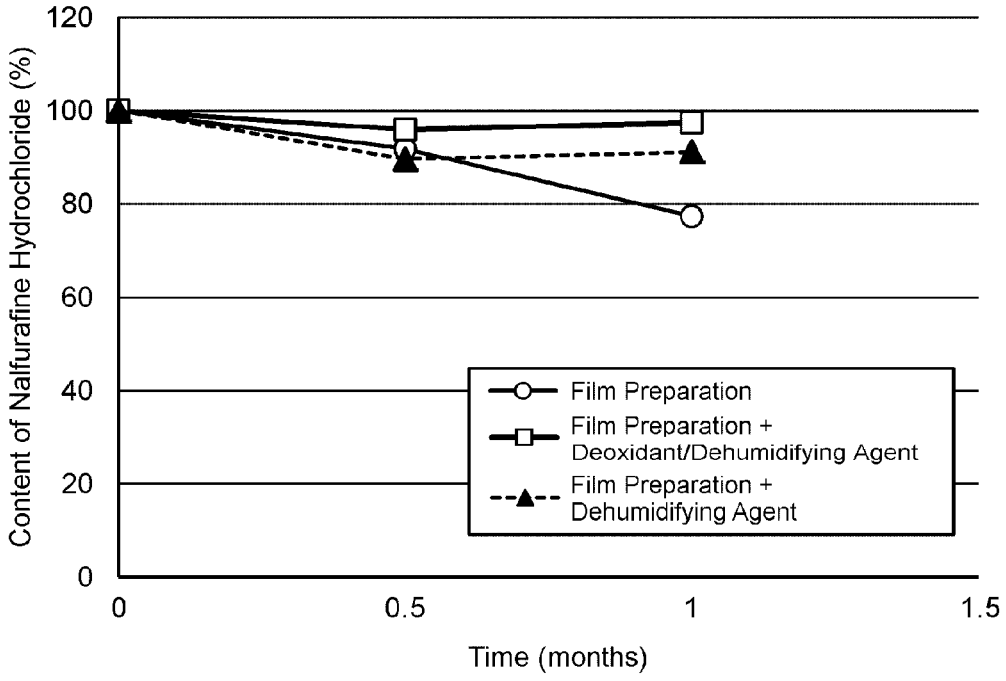
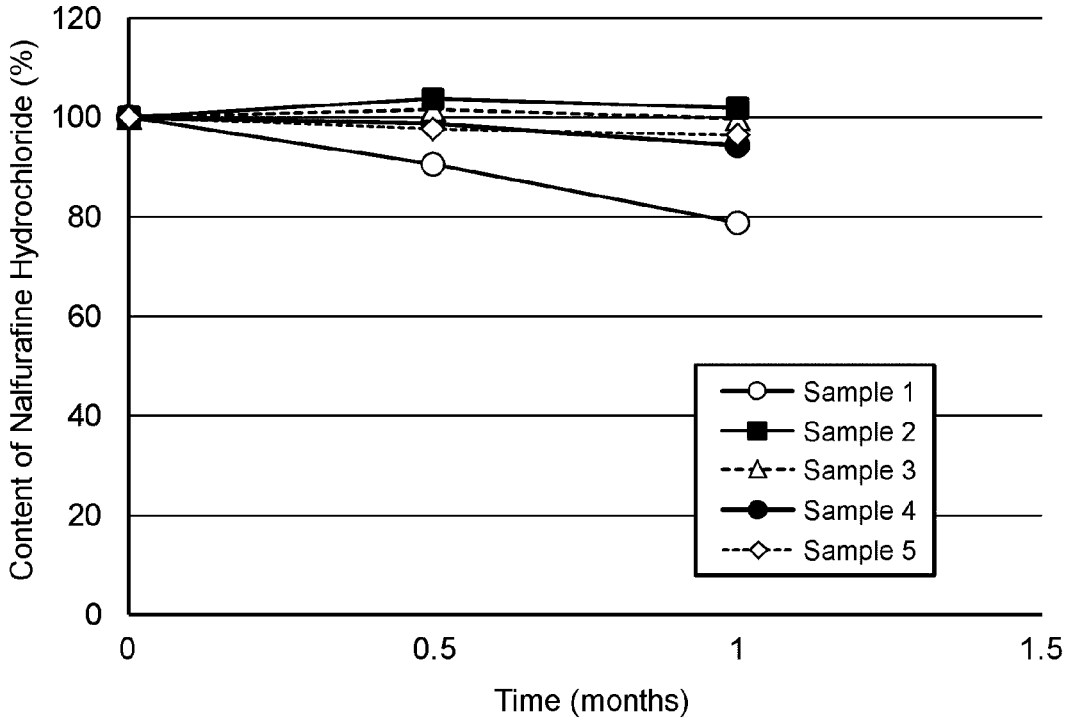

120
100
80
60
40
20
0
Content of Nalfurafine Hydrochloride (%)
0
0.5
1
1.5
Time (months)
Film Preparation
Film Preparation + Deoxidant/Dehumidifying Agent
Film Preparation + Dehumidifying Agent

FIG. 3


120
100
80
60
40
20
0
Content of Nalfurafine Hydrochloride (%)
0
0.5
1
1.5
Time (months)
Sample 1
Sample 2
Sample 3
Sample 4
Sample 5

ORAL FILM PREPARATION

TECHNICAL FIELD

[0001] The present invention relates to an oral film preparation for medical use, in particular to an orally disintegrating film comprising nalfurafine hydrochloride as an active ingredient and being excellent in content uniformity.

BACKGROUND ART

[0002] Generally granules, grains, powders, tablets, capsules, and the like are known as solid preparations of high potency drugs, for example, nalfurafine hydrochloride, and the like. However, in these dosage forms, since a single dose of the high potency drug is very small, the content thereof per unit preparation is very low, and it is difficult to produce a preparation being excellent in content uniformity.

[0003] Patent Document 1 discloses a sheet-like solid drug composition characterized in that the composition is prepared by printing, coating, spraying or injecting a solution or suspension containing a substance having a physiological activation action in a trace amount into a pharmaceutically acceptable sheet-like carrier for the purpose of solving a problem with generation of dusts in a preparation process of a substance having a physiological activation action in a trace amount and an adverse effect thereof on workers and environmental pollution thereby.

[0004] On the other hand, an oral film preparation, especially an oral disintegrating type film preparation has been developed in recent years as one of dosage forms in a pharmaceutical field from the viewpoint of an advantage that it can be taken without water, and portability is satisfactory. However, in the production of an oral film preparation, properties thereof such as brittleness, adhesiveness, and hygroscopicity, and a problem of a lack of uniformity in the interior of the dosage form are recognized (Patent Document 2), and application of an oral film preparation to high potency drugs and evaluation of content uniformity are not known.

PRIOR ART DOCUMENTS

Patent Documents

[0005] Patent Document 1: JP H05-124954 A

[0006] Patent Document 2: JP 2013-527164 A

SUMMARY OF THE INVENTION

Problem to be Solved by the Invention

[0007] In Patent Document 1, a problem with respect to content uniformity is not pointed out and in an application to a carrier by printing, or the like, it is difficult to secure satisfactory content uniformity, and there is room for improvement.

[0008] Therefore, an object of the present invention is to provide an oral film preparation comprising a high potency drug and being excellent in content uniformity, a simple method for producing the film preparation, and a package comprising the oral film preparation and being excellent in stability of the oral film preparation.

Means to Solve the Problem

[0009] The inventors of the present invention have made intensive studies in the light of the above-mentioned problems, and as a result, have found that a high potency drug can be contained in a low content uniformly in an oral film preparation obtained by bringing the high potency drug and a film-forming polymer into a solution state, and spreading and then drying the solution, and have completed the present invention.

[0010] Namely, the present invention relates to:

[1] an oral film preparation obtained by spreading a solution comprising a high potency drug and a film-forming polymer, and then drying the solution,

[2] the oral film preparation of the above [1], wherein the high potency drug is one selected from the group consisting of nalfurafine hydrochloride, veraprost sodium, imidafenacin, limaprost alfadex, lubiprostone and a vitamin D derivative,

[3] the oral film preparation of the above [1] or [2], wherein the film-forming polymer is at least one selected from the group consisting of cellulose, a cellulose derivative, a polyalkylene glycol, an acrylic acid polymer, an acrylic acid copolymer, a methacrylic acid polymer, a methacrylic acid copolymer, a polyacrylamide, a polyvinyl pyrrolidone, a polyvinyl alcohol, a carboxymethyl cellulose, starch, xanthan gum, karaya gum, locust bean gum, tragacanth gum, guar gum, gum acacia, gum arabic, carrageenan, dextrin, dextran, amylose, alginic acid, alginate, a carboxyvinyl polymer, pullulan, chitosan, sodium carboxymethyl starch, *plantago* seed skin, galactomannan, Eudragit, casein, an alginic ester, gelatin, cyclodextrin, a water-soluble pullulan ether (pullulan methyl ether, pullulan ethyl ether, pullulan propyl ether, etc.), a water-soluble pullulan ester (pullulan acetate, pullulan butyrate, etc.), agar, Derakanto, chitin, tara gum, and tamarind gum,

[4] the oral film preparation of any of the above [1] to [3], further comprising at least one plasticizer selected from the group consisting of glycerin, propylene glycol, polyethylene glycol, alkylene glycol, polyalkylene glycol, glycerol, triacetin, deacetylated monoglyceride and triethyl citrate,

[5] the oral film preparation of any of the above [1] to [4], further comprising an antioxidant,

[6] the oral film preparation of any of the above [1] to [5], wherein the oral film preparation is an orally disintegrating film,

[7] a package including the oral film preparation of any of the above [1] to [6], the package being obtained by:

(a) packaging the oral film preparation in a packaging material and after nitrogen substitution, sealing the packaging material, and/or

(b) sealing the oral film preparation together with a deoxidant in a packaging material,

[8] a package obtained by packaging the oral film preparation of any of the above [1] to [6] with a packaging material having a deoxidizing function,

[9] the package of the above [7] or [8], wherein a dehumidifying agent is further sealed, and

[10] a method for producing an oral film preparation comprising a high potency drug, which comprises spreading a solution containing the high potency drug and a film-forming polymer and drying the solution.

Effects of the Invention

[0011] According to the present invention, by spreading a solution containing a high potency drug and a film-forming polymer and then drying the solution, an oral film preparation being excellent in content uniformity of the high potency drug can be provided. From a viewpoint that the oral film preparation can be easily taken without water, the medication compliance can be improved. Further, it is a big advantage for a patient restricted to take water in a limited amount such as a dialysis patient that the administration can be made without water. Furthermore, according to the present invention, stability of the high potency drug can be improved by a package obtained by (a) packaging the oral film preparation in a packaging material and after substitution with nitrogen, sealing the packaging material, and/or (b) sealing the oral film preparation together with a deoxidant in a packaging material, or packaging the oral film preparation with a packaging material having a deoxidizing function. Furthermore, according to the present invention, by spreading a solution containing a high potency drug and a film-forming polymer and then drying the solution, an oral film preparation being excellent in the content uniformity of the high potency drug can be produced by a very simple method.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIG. **1** is a graph showing stability of nalfurafine hydrochloride at a storage temperature of 80° C.

[0013] FIG. **2** is a graph showing stability of nalfurafine hydrochloride at a storage temperature of 60° C.

[0014] FIG. **3** is a graph showing stability of nalfurafine hydrochloride at a storage temperature of 60° C.

EMBODIMENT FOR CARRYING OUT THE INVENTION

[0015] The present invention relates to an oral film preparation comprising a high potency drug as an active ingredient, and is characterized in that the oral film preparation is obtained by spreading a solution containing a high potency drug, a film-forming polymer and a plasticizer into a film shape and then drying the solution.

[0016] In the present invention, the high potency drug means a drug contained in an amount of 0.1 mg or less per one film, and is not particularly limited, and specific examples thereof include nalfurafine hydrochloride, veraprost sodium, imidafenacin, limaprost alfadex, lubiprostone and vitamin D derivatives.

[0017] Nalfurafine hydrochloride is a morphinan compound having a chemical name: (2E)-N-[(5R,6R)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]-3-(furan-3-yl)-N-methylprop-2-enamide monohydrochloride. Nalfurafine hydrochloride is a selective κ-opioid receptor agonist, and exhibits an effect on improvement of pruritus in hemodialysis patients. Currently, nalfurafine hydrochloride is available on the market as REMITCH (registered trademark) CAPSULES 2.5 μg, which is an oral preparation of a soft capsule dosage form. Therefore, it is very beneficial for a patient having a water intake restriction such as a hemodialysis patient that the administration of nalfurafine hydrochloride can be made without water, and since the effect of the present invention can be demonstrated, in the present invention, it is preferable to use nalfurafine hydrochloride as a high potency drug.

[0018] The content of the high potency drug can be easily set by a person skilled in the art, depending on kind and physical properties of an active drug to be used, and, for example, when a nalfurafine hydrochloride is used, usually it is contained in an amount of preferably 0.1 to 80 μg, more preferably 0.5 to 40 μg per one sheet of the film preparation (one dose). When the content of nalfurafine hydrochloride per one sheet of the film preparation exceeds 80 μg, serious side effects tend to develop, and when less than 0.1 μg, there is a tendency that a sufficient medicinal effect cannot be exhibited.

[0019] It is necessary to allow the oral film preparation to contain a film-forming polymer (base material) other than the high potency drug being an active ingredient. Also, if necessary, various additives which are commonly used in the art, i.e. an another plasticizer, a surfactant, a stabilizer, a thickener, an antiseptic agent, an antioxidant, a pH regulator, a die, a pigment, a perfume, a saccharide, a disintegrating agent, an excipient, a flavoring agent, an essential oil, a binder, a moisture-proof agent and the like can be contained within a range not to impair the effects of the present invention.

[0020] It is possible to use, as the film-forming polymer, those which are generally used in the field of film preparation. Specifically, the film-forming polymer is not particularly limited, and examples thereof include water-soluble film-forming polymers such as cellulose, a cellulose derivative, a polyalkylene glycol, an acrylic acid polymer, an acrylic acid copolymer, a methacrylic acid polymer, a methacrylic acid copolymer, a polyacrylamide, a polyvinyl pyrrolidone, a polyvinyl alcohol, a carboxymethyl cellulose, starch, xanthan gum, karaya gum, locust bean gum, tragacanth gum, guar gum, gum acacia, gum arabic, carrageenan, dextrin, dextran, amylose, alginic acid, alginate, a carboxyvinyl polymer, pullulan, chitosan, sodium carboxymethyl starch, *plantago* seed skin, galactomannan, Eudragit, casein, an alginic ester, gelatin, cyclodextrin, a water-soluble pullulan ether (pullulan methyl ether, pullulan ethyl ether, pullulan propyl ether, etc.), a water-soluble pullulan ester (pullulan acetate, pullulan butyrate, etc.), agar, Derakanto, chitin, tara gum, and tamarind gum, and a mixture thereof.

[0021] Examples of the cellulose derivatives include alkyl celluloses such as methyl cellulose and ethyl cellulose; substituted alkyl celluloses such as hydroxyethyl cellulose, hydroxypropyl cellulose (HPC), hypromellose (hydroxypropyl methyl cellulose) (HPMC), hydroxypropyl methyl cellulose phthalate (HPMCP) and carboxymethyl ethyl cellulose (CMEC); salts of substituted alkyl celluloses such as potassium carboxymethylcellulose, sodium carboxymethylcellulose and calcium carboxymethylcellulose; cellulose acetate phthalate (CAP), and the like, and mixtures thereof.

[0022] The content of the film-forming polymer is not particularly limited, and is preferably 30% by mass or more, more preferably 40% by mass or more in the oral film preparation. When the content of the film-forming polymer is less than 30 parts by mass, there is a tendency that the film becomes brittle, thereby causing a problem with the film quality.

[0023] The plasticizers are not limited particularly, and examples thereof include alkylene glycol, polyalkylene glycol, glycerol, triacetin, deacetylated monoglyceride, polyethylene glycol, triethyl citrate and the like. These plasticizers may be used alone or may be used in combination of two or more kinds thereof.

[0024] When the plasticizer is contained in the oral film preparation, the content thereof is not particularly limited, and is preferably 40% by mass or less, more preferably 30% by mass or less. When the content of the plasticizer exceeds 40% by mass, there is a tendency that sufficient strength cannot be maintained and thereby a film cannot be formed. The content of the plasticizer in the oral film preparation is preferably 0.1% by mass or more, more preferably 0.5% by mass or more. When the content of the plasticizer is less than 0.1% by mass, there is a possibility that flexibility of the preparation is not obtained, which has an adverse effect on quality thereof.

[0025] Examples of the antioxidant include ascorbic acid, bisulfite, sulfite, dibutylhydroxytoluene (BHT), natural vitamin E, tocopherol, d-delta-tocopherol, tocopherol acetate, concentrated mixed tocopherol, thiosulfate, propyl gallate, pyrosulfite, nitrite, L-ascorbyl stearate, α-thioglycerol, edetate, erythorbic acid, cysteine hydrochloride, citrate, dichloroisocyanurate, soya lecithin, thioglycolate, thiomalate, ascorbyl palmitate, butylhydroxyanisole, 1,3-butylene glycol, benzotriazole, pentaerythrityl-tetrakis[3-(3,5-di-t-butyl-4-hydroxyphenyl)propionate], 2-mercaptobenzimidazole, and the like.

[0026] When the antioxidant is contained in the oral film preparation, the content thereof is not particularly limited, and is preferably 70% by mass or less, more preferably 60% by mass or less. When the content of the antioxidant exceeds 70% by mass, a flavor is impaired due to taste and odor peculiar to the antioxidant, and there is a case where quality of the preparation is deteriorated. The content of the antioxidant in the oral film preparation is preferably 0.0001% by mass or more, more preferably 0.001% by mass or more, further preferably 0.01% by mass or more. When the content of the antioxidant is less than 0.0001% by mass, there is a possibility that a sufficient antioxidation effect cannot be obtained, which has an adverse effect on quality thereof.

[0027] Particularly in terms of content uniformity, the oral film preparation according to the present invention can be produced by applying a uniform solution including a film-forming polymer, a plasticizer and active ingredients in a predetermined thickness and then drying the solution. More specifically, an oral film preparation having a thickness, for example, within a range of 5 to 400 μm, preferably within a range of 10 to 300 μm can be obtained by (1) dissolving the film-forming polymer and the additives such as a plasticizer in a mixed solvent of water and an alcohol to obtain a solution, (2) dissolving a drug as an active ingredient in water, (3) kneading the solutions of (1) and (2) to obtain a drug solution, and (4) spreading the obtained drug solution in a predetermined thickness and then drying the solution.

[0028] In the present invention, the oral film preparation can be easily taken without water, and therefore, is preferably an orally disintegrating film from the viewpoint that an improvement of medication compliance by prevention of erroneous swallowing by a dysphagia patient can be expected, and that moisture management for a dialysis patient having a water intake restriction can be expected to be easily performed. The orally disintegrating film can be produced by appropriately combining the film forming polymer and the plasticizer described above. Example thereof includes one comprising hydroxypropyl cellulose and hypromellose as suitable film-forming polymers and polyethylene glycol as a plasticizer.

[0029] In the present invention, in the case of using a drug to be affected by oxidation, especially nalfurafine hydrochloride as an active ingredient, it was confirmed that by taking deoxidation means, the degradation of the active ingredient can be reduced and the stable preparation can be obtained.

[0030] Examples of such a deoxidizing means include a method for allowing an antioxidant to be contained in the above-mentioned oral film preparation, a method for conducting substitution with nitrogen at the time of packaging, a method for sealing a deoxidant in the package, and a method of using a packaging material, for example, a packaging film having a deoxidizing function, and the method of using a packaging material having a deoxidizing function is preferable from the viewpoint of easy extraction of a preparation from a packaging material, cost reduction of starting materials, and simplification of a manufacturing process.

[0031] Examples of the deoxidant allowed to coexist in the package include inorganic deoxidants such as iron and cerium oxide, organic deoxidants and the like, and one having a flat form such as a sheet-like or a stick-like shape similar to the oral film preparation of the present invention is preferable. Such a deoxidant is not particularly limited, and there are commercially available deoxidants usable for pharmaceutical applications, for example, "PharmaKeep" manufactured by Mitsubishi Gas Chemical Company, Inc., and "AGELESS" manufactured by Mitsubishi Gas Chemical Company, Inc.

[0032] The packaging material having a deoxidizing function is not particularly limited, and a packaging film including a deoxidant is preferable. Such a packaging film can be classified into one including an inorganic deoxidant such as iron or cerium oxide, or an organic deoxidant-containing film. These films are not particularly limited, and examples thereof include commercially available films that can be used for pharmaceutical applications, and for example, "OxyCatch (registered trademark)" manufactured by Kyodo Printing Co. Ltd. and "High Star 02" manufactured by Starplastic Industry Inc. can be used as a packaging material containing cerium oxide, and "AGELESS OMAC (registered trademark)" manufactured by Mitsubishi Gas Chemical Company, Inc. and "Oxyguard" manufactured by Toyo Seikan Co., Ltd. can be used as a packaging material containing iron.

[0033] Furthermore, in the oral film preparation of the present invention, even when the drug in the film cannot be kept sufficiently stable with only a deoxidizing means, there is a case where the drug in the film can be stably maintained by combination use of a dehumidifying agent. In such a case, combination use of the dehumidifying agent is preferable. It is a matter of course to allow a dehumidifying agent having only a dehumidifying function to coexist with the preparation in the package which is made by packaging with a packaging material having a deoxidizing function, and a dehumidifying agent commonly used in the field of pharmaceuticals can be used as such a dehumidifying agent.

[0034] In yet another embodiment, the present invention relates to a method for producing an oral film preparation containing a high potency drug. The method for producing an oral film preparation containing a high potency drug of the present invention is characterized by using a solution containing a film-forming polymer in which a high potency drug is dissolved, and comprises spreading and drying the

solution. For example, as described above for the oral film preparation of the present invention, the producing method of the present invention can be performed specifically by a step 1 of dissolving the film-forming polymer and optionally other additives in a solvent such as water; a step 2 of dissolving the high potency drug in a solvent such as water; a step 3 of obtaining a solution containing the high potency drug and the film-forming polymer by kneading the solution obtained in the step 1 and the solution obtained in the step 2; a step 4 of spreading the solution obtained in the step 3 on a liner or the like in a predetermined thickness if necessary; a step 5 of drying the spread solution; and a step 6 of cutting the dried film to an appropriate size; and the like.

[0035] The above description made for the "oral film preparation" is also applied similarly to the "method for producing an oral film preparation containing a high potency drug" unless otherwise contradictory, and further, the above description made for the "method for producing an oral film preparation containing a high potency drug" is also applied similarly to the above-mentioned "oral film preparation".

[0036] The present invention is described in more detail by means of Examples and Comparative Examples, but the present invention is not limited to these Examples.

EXAMPLE

[0037] Ingredients used in Examples and Comparative Examples are those described in Japanese Pharmacopoeia or Japanese Pharmaceutical Excipients.

Examples 1 to 4

[0038] According to the formulation in Table 1, (a) hydroxypropyl cellulose, hypromellose and propylene glycol were added to a mixed solution of water and ethanol, followed by stirring at room temperature for 30 minutes to be dissolved in the solution (Solution A); (b) nalfurafine hydrochloride was added to an appropriate amount of water (except one in Table 1), followed by stirring at room temperature for 5 minutes to be dissolved in the water (Solution B); and (c) the Solution A of (a) and the Solution B of (b) were mixed and the mixture was kneaded at room temperature for 30 minutes using a three-one motor to obtain a Drug Solution C.

[0039] The obtained Drug Solution C was coated uniformly on a liner so that the coating thickness after drying became 40 μM, followed by drying at 70° C. for 10 minutes in Example 1, at 80° C. for 10 minutes in Example 2, at 80° C. for 15 minutes in Example 3, and at 80° C. for 30 minutes in Example 4. The obtained films were punched into a size of 1.5×2.0 cm (3.0 cm^2) to obtain film preparations. A theoretical mass of the obtained film preparation per sheet was 12 mg, and the drug content was 2.5 μg.

TABLE 1

Composition	Charged amount (g)	Dry mass %
Nalfurafine hydrochloride	0.002083	0.02083
HPC	4.499	44.98959
HPMC	4.499	44.98959
PEG400	1.00	10.00
Ethanol	28.33	0.00
Water	28.33	0.00

Example 5

[0040] According to the formulation in Table 2, (a) hydroxypropyl cellulose, hypromellose, propylene glycol and an antioxidant (sodium sulfite) were added to a mixed solution of water and ethanol, followed by stirring at room temperature for 30 minutes to be dissolved in the solution (Solution A); (b) nalfurafine hydrochloride was added to an appropriate amount of water (except one in Table 2), followed by stirring at room temperature for 5 minutes to be dissolved in the water (Solution B); and (c) the Solution A of (a) and the Solution B of (b) were mixed and the mixture was kneaded at room temperature for 30 minutes using a three-one motor to obtain a Drug Solution C.

[0041] The obtained Drug Solution C was coated uniformly on a liner so that the coating thickness after drying became 40 μm, followed by drying at 80° C. for 15 minutes. The obtained film was punched into a size of 1.5×2.0 cm (3.0 cm^2) to obtain a film preparation. A theoretical mass of the obtained film preparation per sheet was 12 mg, and the drug content was 2.5 μg.

TABLE 2

Composition	Charged amount (g)	Dry mass %
Nalfurafine hydrochloride	0.002083	0.02083
HPC	4.399	43.98959
HPMC	4.399	43.98959
PEG400	1.00	10.00
Sodium sulfite	0.20	2.00
Ethanol	28.33	0.00
Water	28.33	0.00

Test Example 1 (Content Uniformity Test)

[0042] For the film preparations obtained in Examples 1 to 4 (n=3 in each of Examples), the concentrations of the drug of the three sheets of film preparations per one lot were measured to calculate an average value and a standard deviation. A relative standard deviation was calculated as an index for the content uniformity from the calculated average value and standard deviation. The results are shown in Table 3.

TABLE 3

Example	Actual value (%)	Concentration (%)	RSD
1	102.6	101.9	0.32
2	102.6	103.5	1.97
3	103.4	102.8	2.19
4	104.2	103.2	0.61

[0043] From Table 3, it is seen that in any of Examples, the relative standard deviation is less than 2.2 and the content uniformity is excellent.

Test Example 2 (Stability Test)

[0044] A film preparation produced in the same manner as in Example 3 was sealed as it was or together with a deoxidant/dehumidifying agent (PharmaKeep (KD-20) manufactured by Mitsubishi Gas Chemical Company, Inc.) in Easy Peel (manufactured by Toppan Printing Co., Ltd.), or sealed in a packaging material having a dehumidifying function (Moisture Guard (MG) manufactured by Toyo

Seikan Co., Ltd.), followed by storing in a thermostat of 80° C. The content of the drug (nalfurafine hydrochloride) in the preparation was measured when starting the storing and during the storing (three days after and seven days after). The results are shown in FIG. **1** as a drug content (%) assuming that the drug content when starting the storing is 100.

Test Example 3 (Stability Test)

[0045] The content of the drug (nalfurafine hydrochloride) was measured in the same manner as in Test Example 2 except that the storing temperature was changed to 60° C. and during the storing, measurement was made 0.5 month after and one month after. The results are shown in FIG. **2** as a drug content (%) assuming that the drug content when starting the storing is 100.

Test Example 4 (Stability Test)

[0046] The film preparation was sealed in a packaging material shown in Table 4, and stored in a thermostat of 60° C. Film preparations produced in the same manner as in Example 3 were used as Samples 1 to 4, and the film preparation produced in Example 5 was used as Sample 5. The contents of the drug (nalfurafine hydrochloride) in the preparation were measured when starting the storing and during the storing (0.5 month after and one month after). The results are shown in FIG. **3** as a drug content (%) assuming that the drug content when starting the storing is 100.

TABLE 4

Sample No.	Packaging material (front)	Packaging material (back)	Antioxidant
1	Easy Peel *1	Easy Peel	—
2	OxyCatch *2	Easy Peel	—
3	OxyCatch	OxyCatch	—
4	AGELESS OMAC *3	AGELESS OMAC	—
5	Easy Peel	Easy Peel	2% Sodium sulfite

*1 Packaging material manufactured by Toppan Printing Co., Ltd.

*2 Packaging material including cerium oxide manufactured by Kyodo Printing Co., Ltd.

*3 Packaging material including iron manufactured by Mitsubishi Gas Chemical Company, Inc.

[0047] It is seen from FIGS. **1** to **3** that the oral film preparation of the present invention assures that stability of the drug can be maintained even in the case of a long-term storage thereof by taking a deoxidizing means.

1. An oral film preparation obtained by spreading a solution containing a high potency drug and a film-forming polymer and drying the solution.

2. The oral film preparation of claim **1**, wherein the high potency drug is one selected from the group consisting of nalfurafine hydrochloride, veraprost sodium, imidafenacin, limaprost alfadex, lubiprostone and a vitamin D derivative.

3. The oral film preparation of claim **1**, wherein the film-forming polymer is at least one selected from the group consisting of cellulose, a cellulose derivative, a polyalkylene glycol, an acrylic acid polymer, an acrylic acid copolymer, a methacrylic acid polymer, a methacrylic acid copolymer, a polyacrylamide, a polyvinyl pyrrolidone, a polyvinyl alcohol, a carboxymethyl cellulose, starch, xanthan gum, karaya gum, locust bean gum, tragacanth gum, guar gum, gum acacia, gum arabic, carrageenan, dextrin, dextran, amylose, alginic acid, alginate, a carboxyvinyl polymer, pullulan, chitosan, sodium carboxymethyl starch, *plantago* seed skin, galactomannan, Eudragit, casein, an alginic ester, gelatin, cyclodextrin, a water-soluble pullulan ether (pullulan methyl ether, pullulan ethyl ether, pullulan propyl ether, etc.), a water-soluble pullulan ester (pullulan acetate, pullulan butyrate, etc.), agar, Derakanto, chitin, tara gum, and tamarind gum.

4. The oral film preparation of claim **1**, further comprising at least one plasticizer selected from the group consisting of glycerin, propylene glycol, polyethylene glycol, alkylene glycol, polyalkylene glycol, glycerol, triacetin, deacetylated monoglyceride and triethyl citrate.

5. The oral film preparation of claim **1**, further comprising an antioxidant.

6. The oral film preparation of claim **1**, wherein the oral film preparation is an orally disintegrating film.

7. A package including the oral film preparation of claim **1**, the package being obtained by

(a) packaging the oral film preparation in a packaging material and after nitrogen substitution, sealing the packaging material, and/or

(b) sealing the oral film preparation together with a deoxidant in a packaging material.

8. A package obtained by packaging the oral film preparation of claim **1** with a packaging material having a deoxidizing function.

9. The package of claim **7**, wherein a dehumidifying agent is further sealed.

10. A method for producing an oral film preparation comprising a high potency drug, which comprises spreading a solution containing the high potency drug and a film-forming polymer and drying the solution.

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