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(54) **Title**: TASTE MASKED PHARMACEUTICAL COMPOSITIONS OF PREGABALIN

(57) **Abstract**: The invention provides taste masked pharmaceutical compositions comprising pregabalin or salts or enantiomers thereof. The invention also relates to the process of preparation of such compositions.

TASTE MASKED PHARMACEUTICAL COMPOSITIONS OF PREGABALIN

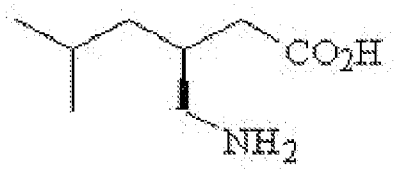
Field of the Invention

The invention provides taste masked pharmaceutical compositions comprising pregabalin or salts or enantiomers thereof. The invention also provides process for preparation of such compositions.

Background of the Invention

Pregabalin reduces calcium influx into the nerve terminals by binding to the α2δ (alpha2delta) subunit of the voltage-dependent calcium channel in the central nervous system. Pregabalin also decreases the release of neurotransmitters such as glutamate, noradrenaline. Pregabalin increases neuronal GABA levels by producing a dose-dependent increase in glutamic acid decarboxylase activity.

Chemically, pregabalin is (S)-3-(aminomethyl)-5-methylhexanoic acid having a structure of Formula I. Pregabalin is used particularly in the treatment of management of neuropathic pain associated with diabetic peripheral neuropathy, management of postherpetic neuralgia, adjunctive therapy for adult patients with partial onset seizures and management of fibromyalgia.



FORMULA I

U.S. Patent No. 6,197,819 discloses pharmaceutically acceptable salt of S-(+)-(4)-amino-3-(2-methylpropyl) butanoic acid, said salt being present as a single optical isomer.

U.S. Patent No. 5,563,175 discloses method of treating a patient having seizure disorders using pregabalin.

U.S. Patent No. 6,001,876 discloses method for treating pain-using pregabalin.

U.S. Patent No. 6,488,964 discloses process for manufacturing coated particles of gamma-aminobutyric acid analogue.

U.S. Patent No. 6,660,382 discloses method for making coated granules with masked taste and instant release of the active principle.

U.S. Patent No. 7,022,678 discloses pregabalin lactose conjugate compounds.

U.S. Patent Application No. 20050171203A1 discloses orally administrable aqueous pharmaceutical composition containing pregabalin.

U.S. Application No. 20070269511A1 disclose solid pharmaceutical composition containing pregabalin in the form of matrix.

U.S. Application No. 20090082400 discloses a stable aqueous composition comprising cyclodextrin.

Pregabalin is a BCS Class 1 compound, rapidly absorbed when administered on an empty stomach, with peak plasma concentrations occurring within one hour, not bound to plasma proteins.

Pregabalin is administered by oral route, however bitter taste is major drawback of pregabalin. It is essential to mask the taste of pregabalin at least while they are in the oral cavity, so as to make them more pleasant and to optimize the better patient's compliance.

Current dosing of pregabalin is twice a day using immediate release capsule (Lyrica®). The capsule forms, are however difficult to swallow, especially for geriatric patients. Further, the fear of swallowing, or choking on such solid shaped articles is still a concern

in certain populations especially geriatrics. It is estimated that almost 50% of the population have problems of swallowing tablets or capsules (Seager in Journal of Pharmacol. And Pharm. Pages 375-382, 1998). Capsule dosage forms become sticky when wetted by saliva, and if patient experiences difficulty in swallowing on first attempt, then the capsule must often be discarded. Furthermore, if a capsule partially dissolves in patient's mouth, as can result from unsuccessful swallowing or the capsule getting stuck in the orthodontic appliance, the resulting unpleasant taste can make it difficult to persuade the patient to take another dose. Additionally, these dosage forms are difficult to carry, store and handle. Moreover, the difficulties associated with capsules result in decreased patient compliance.

Further, capsule dosage form available in the market takes more time to disintegrate and hence in turn delays onset of action. Hence there is a need for quick release dosage form of pregabalin so that it initiates faster dissolution and in turn faster action than the Lyrica® capsules.

Summary of the Invention

In one of the aspects of the present invention, there is provided a taste masked pharmaceutical composition of pregabalin or salts or enantiomers thereof, wherein the taste masking is achieved by using one or more of ion exchange resins or methacrylate polymers or cyclodextrins or derivatives thereof.

The term "Ion exchange resins" as used herein refers to highly ionic, covalently cross-linked, insoluble polyelectrolytes.

One of the embodiments of the pharmaceutical composition may include one or more of the following features. The pharmaceutical composition may further comprises one or more pharmaceutically acceptable excipients selected from the group consisting of one or more of binders, fillers, disintegrants, glidants, lubricants, surfactants, sweeteners and flavors.

In another aspect of the present invention, there is provided a quick release pharmaceutical composition comprising pregabalin or salts or enantiomers thereof, wherein the composition releases not less than about 60% of the dose in 30 min when tested for dissolution using United States Pharmacopoeia Apparatus 2, paddles@ 50 rpm in 900 mL of 0.06 N HCl.

Embodiments of the quick release pharmaceutical composition may include one or more of the following features. The quick release pharmaceutical composition can be present in different dosage forms suitable for oral administration. The quick release pharmaceutical compositions may be taste masked using one or more ion exchange resins or methacrylate polymers or cyclodextrins or derivatives. The quick release composition may further comprises one or more of binders, fillers, disintegrants, glidants, lubricants, surfactants, sweeteners and flavors.

Description of drawings

Figure 1: Comparative dissolution profile of pregabalin chewable tablets and Lyrica®

Detailed Description of the Invention

We have now discovered that the taste masking composition of pregabalin is achieved by the use of one or more ion exchange resins or methacrylate polymers or cyclodextrins or derivatives thereof. While working on pregabalin composition, the present inventors have found that when methacrylate polymers are used as taste masking agent with pregabalin, the resulting product is taste masked and better patient compliant. Further, inventors have also found that ion exchange resins also act as good taste masking agent when complexed with pregabalin. Use of cyclodextrins or derivatives thereof along with pregabalin not only results in taste masking but also increases the solubility of the complex formed in aqueous solution. The taste-masked pregabalin is then incorporated with other excipients to formulate various dosage forms using flavors and other ingredients.

In one of the embodiments of the present invention, taste masking of pharmaceutical composition comprising pregabalin or salts or enantiomers is achieved by using one or more ion exchange resin.

Ion exchange resins are commonly prepared from the styrene and various levels of the cross-linking agent divinyl benzene. When the resin is immersed in a medium in which it is insoluble, the counter ions are mobile and can be exchanged for the other counter ions from the surrounding medium and thus form the complex.

The ion exchange resins comprise cation exchange resins or anion exchange resins comprising one or more of polacrilex resin, polacrilin potassium, sodium polystyrene sulfonated or cholestyramine resin.

In one of the embodiments of the present invention, taste masking of pharmaceutical composition comprising pregabalin or salts or enantiomers is achieved by using one or more methacrylate polymers.

In another embodiments of the present invention, the methacrylate polymers comprise one or more of Eudragit E100 or Eudragit EPO.

In one of the embodiments of the present invention, the taste masked pharmaceutical composition comprises an inclusion complex of pregabalin or pharmaceutically acceptable salt with cyclodextrin or derivative thereof.

In another embodiments of the present invention, the taste masked pharmaceutical composition comprises an admixture of pregabalin or pharmaceutically acceptable salt with cyclodextrin or derivative thereof.

The term “admixture” refers to a state produced by a process comprising mixing pregabalin or salts pr enantiomers thereof with cyclodextrin or derivatives thereof.

Cyclodextrins are cyclic oligosaccharides of a-D-gluco-pyranose containing a relatively hydrophobic central cavity and hydrophilic outer surface. Cyclodextrins, also called "Schardingers dextrins", cycloamyloses, cyclomaltoses and cycloglucans, are oligomers of anhydroglucose, bonded together by alpha 1,4 bonds to form a ringed compound. A six membered ring is called alpha cyclodextrin; seven, beta cyclodextrin, and eight, gamma cyclodextrin. These six, seven and eight membered rings are also referred to as cyclomaltohexaose, cyclomaltoheptaose and cyclomaltoctaose, respectively.

Cyclodextrins and their derivatives are a class of substances that is successfully used for oral or parenteral formulation of poorly soluble pharmaceutical substances. The interior of the cyclodextrin molecule is hydrophobic while the exterior is sufficiently hydrophilic to allow the cyclodextrin to be dissolved in water. This difference between the interior and exterior faces allows the cyclodextrin to act as a host molecule and to form inclusion complexes with poorly soluble pharmaceutical substances. By the formation of an inclusion complex in the hydrophobic interior space of the cyclodextrin, an increased solubility of poorly water-soluble pharmaceutical substances is achieved. This in turn results in a faster rate of solution and can contribute to an increase in bioavailability.

In the pharmaceutical industry, cyclodextrins or derivatives thereof have mainly been used as complexing agents to increase the aqueous solubility of poorly water-soluble drugs, and to increase their bioavailability and stability. Light, thermal and oxidative stability of actives may be improved through the formation of cyclodextrin complexes. In addition, cyclodextrins or derivatives thereof are used to reduce or prevent gastrointestinal or ocular irritation, reduce or eliminate unpleasant smells or tastes, prevent drug-drug or drug-additive interactions, or even to convert oils and liquid drugs into microcrystalline or amorphous powders. Incorporation of cyclodextrin in the composition also prevents discoloration of the dosage form.

In another embodiment of the present invention, the cyclodextrin or derivatives thereof are selected from the group consisting of α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, hydroxypropyl- α–cyclodextrin, hydroxypropyl-β-cyclodextrin, dimethyl – β-

cyclodextrin, 2-hydroxyethyl β –cyclodextrin, trimethyl -β –cyclodextrin, and sulfonated cyclodextrins, in anhydrous or hydrated form.

In one of the embodiments of the present invention, the quick release pharmaceutical composition is taste masked. Taste masking is achieved by using one or more of ion exchange resins or methacrylate polymers or cyclodextrins or derivatives thereof.

In another embodiment of the invention the quick release pharmaceutical composition releases not less than about 80% of the dose in 30 minutes when the composition is tested for dissolution using United States Pharmacopoeia Apparatus 2, paddles@ 50 rpm in 900 mL of 0.06 N HCl.

In another embodiment of the present invention, the taste masked pregabalin composition further comprises one or more pharmaceutically acceptable excipients selected from the group consisting of one or more of binders, fillers, disintegrants, glidants, lubricants, surfactants, sweeteners and flavors.

Suitable binder may include one or more of povidone, starch, stearic acid, gums, celluloses, alginic acids, chitosan, chitin or polyethylene glycol.

Suitable filler may include one or more of saccharose, glucose, fructose, maltose, maltitol, mannitol, dextrins such as maltodextrins; xylitol, sorbitol, microcrystalline cellulose, calcium phosphate, calcium sulfate, kaolin, dry starch, powdered sugar or silicates such as magnesium aluminium silicate.

Suitable disintegrant may include one or more of starch, pregelatinized starch, croscarmellose sodium, crospovidone or sodium starch glycolate.

Suitable glidant may include one or more of colloidal silicon dioxide, talc or cornstarch.

Suitable lubricant may include one or more of magnesium stearate, zinc stearate, calcium stearate, stearic acid, sodium stearyl fumarate, hydrogenated vegetable oil or glyceryl behenate.

Suitable surfactants are those known to ordinary skilled in the art and may include but not limited to amphoteric, non-ionic, cationic or anionic surfactants. Suitable surfactants comprises one or more of sodium lauryl sulfate, monooleate, monolaurate, monopalmitate, monostearate or another ester of polyoxyethylene sorbitane, sodium dioctylsulfosuccinate (DOSS), lecithin, stearylic alcohol, cetostearylic alcohol, cholesterol, polyoxyethylene ricin oil, polyoxyethylene fatty acid glycerides, poloxamer or cremophore RH 40.

Suitable sweetener may include one or more of monosaccharides, disaccharides and polysaccharides, e.g. xylose, ribose, glucose, mannose, galactose, fructose, sucrose, maltose, invert sugar, partially hydrolyzed starch, corn syrup solids, mannitol, xylitol, D-sorbitol, erythritol, pentitol, hexitol, malitol, dihydrochalcones, monellin, steviosides or glycyrrhizin; saccharin in free acid form, soluble saccharin salts, e.g. sodium or calcium saccharin salts, cyclamate salts or acesulfame K; dipeptide based sweeteners, such as L-aspartic acid derived sweeteners, e.g. aspartame; water-soluble sweeteners derived from naturally occurring water-soluble sweeteners, e.g. sucralose; and protein based sweeteners, e.g. thaumatococcus danielli (Thaumatin I and II).

Suitable flavoring agents may include those known to the skilled artisan, such as natural, "natural-like" and artificial flavors. These flavors may be chosen e.g. from synthetic flavor oils, flavoring aromatics, oleo-resins and extracts derived e.g. from plants, leaves, flowers or fruits.

Representative flavors may include one or more of spearmint oil, cinnamon oil, peppermint oil, clove oil, bay oil, thyme oil, cedar leaf oil, oil of nutmeg, oil of sage, oil of bitter almonds, vanilla, chocolate, coffee, cocoa and citrus oil, lemon, orange, cherry, grape, lime or grapefruit, and fruit essences, e.g. apple, pear, peach, strawberry,

raspberry, cherry, plum, pineapple or apricot; mints such as peppermint (including menthol, especially levomenthol), aldehydes and esters, e.g. cinnamyl acetate, cinnamaldehyde, citral, diethylacetal, dihydrocarvyl acetate, eugenyl formate or p-methylanisol; alpha-citral (geranial) and beta-citral (neral); decanal; ethyl vanillin; piperonal (heliotropine); vanillin; alpha-amyl cinnamaldehyde; butyraldehyde; valeraldehyde; citronellal; decanal; aldehyde C-8; aldehyde C-9; aldehyde C-12; 2-ethyl butyraldehyde; hexenal, i.e. trans-2; tolyl aldehyde; veratraldehyde; 2,6-dimethyl-5-heptenal (melonal); or 2-6-dimethyloctanal; 2-dodecenal.

Moreover, compositions of the invention optionally include usual auxiliaries known in the art such as saliva stimulating agents like citric acid, lactic acid, malic acid, succinic acid, ascorbic acid, adipic acid, fumaric acid, tartaric acids; cooling sensation agents like maltitol, monomenthyl succinate, ultracool; stabilizers like gums, agar; taste masking agents like acrylic polymers, copolymers of acrylates, celluloses, resins; coloring agents like titanium dioxide, natural food colors, dyes suitable for food, drug and cosmetic applications; preservatives like alpha-tocopherol, citric acid, butylated hydroxytoluene, butylated hydroxyanisole, ascorbic acid, fumaric acid, malic acid, sodium ascorbate or ascorbic acid palmitate or effervescing agents like citric acid, tartaric acid, sodium bicarbonate or sodium carbonate.

The pharmaceutical composition of the present invention can be present in the form of tablet, capsule, powder, disc, caplet, granules, pellets, granules in capsule, minitablets, minitablets in capsule, pellets in capsule, sachet, orally disintegrating tablet, chewable tablet, effervescent tablet, mouth dissolving film, syrup, solution, suspension, elixir, emulsion and other dosage forms suitable for oral administration.

The tablet may vary in shapes such as oval, round, triangle, almond, peanut, pentagonal, trapezoidal or parallelogram.

In one of the embodiments of the invention, the quick release composition is an orally disintegrating tablet. The hardness of the tablet is in the range of about 15 Newtons to about 70 Newtons.

In another embodiment of the invention, the quick release composition is chewable tablet.

The pharmaceutical composition of the invention may be prepared by physical mixing, wet mixing, spray congealing, hot melt, antisolvent, microfluidization, spray drying and freeze drying.

The pharmaceutical composition of the invention may be prepared by mixing pregabalin or salts or enantiomers thereof with other pharmaceutically acceptable excipients, and optionally compressing the mixture into tablets.

The pharmaceutical composition of the invention may also be prepared by suspending mixture of pregabalin or enantiomers or salts thereof with other pharmaceutically acceptable excipients in surfactant solution and granulating the mixture of other pharmaceutically acceptable excipients with said suspension, drying the granules, optionally compressing the granules into tablets.

Dissolution studies are performed using United States Pharmacopoeia Apparatus 2, paddles@ 50 rpm in 900 mL of 0.06N HCl. Samples are withdrawn at different time interval for analyzing the percentage drug released. Fig. 1 illustrates the dissolution profile of taste masked pregabalin composition.

While the present invention has been described in terms of its specific embodiments, certain modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention.

The invention is further illustrated by the following examples which are provided merely to be exemplary of the invention and do not limit the scope of the invention. Certain

modifications and equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the invention.

Example 1: Orally Disintegrating Tablet of Pregabalin

Table 1: Composition of Pregabalin Orally Disintegrating Tablet

S.No.	Ingredients	(% w/w)
Intragranular		
1	Pregabalin	20-60
2	Eudragit EPO	5-40
Extragranular		
3	Mannitol SD 200	5-30
4	Starlac	5-30
5	Ac-di-sol	1-15
6	Sucralose	1-10
7	Cinnamon flavour	1-10
8	Magnesium stearate	0.5-5

Procedure: Pregabalin was granulated with aqueous solution of Eudragit EPO. Granules were dried, mixed with Mannitol, Ac-di-sol, Sucralose, Cinnamon flavour and lubricated by magnesium stearate. The lubricated blend was compressed into suitable sized tablets using suitable tooling.

Example 2: Orally disintegrating tablets as exemplified in Example 1 were evaluated for its hardness, friability and disintegration time using standard techniques. The results obtained are enumerated in Table 2.

Table 2: Evaluation of hardness, friability and disintegration time

Test	Results
Hardness (N)	40-50
Friability (%)	0.1%
Disintegration Time (sec)	45

Example 3: Chewable tablets of Pregabalin

Table 3: Composition of Pregabalin Chewable Tablets

S. No.	Ingredients	(% w/w)
Intragranular		
1.	Pregabalin	20-60
2.	Eudragit EPO	5-45
3.	Talc	0.5-10
4.	Sucralose	0.5-5
Extragranular		
5.	Avicel 101	5-40
6.	Prosolv SMCC-50 (Silicified Microcrystalline Cellulose)	5-30
7.	Aspartame	1-10
8.	Novamint	1-10
9.	Aerosil	1-5
10.	Talc	0.5-10

Procedure: Eudragit EPO was dissolved in a suitable vehicle and to it sucralose and talc were added. Pregabalin was granulated using the above Eudragit EPO solution in rapid mixer granulator. The granules obtained were dried. Dried granules were mixed with Avicel 101, Prosolv –50, Aspartame, and mint. Aerosil and talc was added to above powder blend. The lubricated powder blend was then compressed to a tablets using suitable tooling.

Example 4: Dissolution studies

Dissolution studies were performed using chewable tablets of example 3 and Lyrica® in United States Pharmacopoeia Apparatus 2 in 900ml of 0.06N HCl media with a paddle speed of 50 rpm. Samples from the dissolution apparatus were withdrawn at 0min, 10min, 20min, 30min and 45min and were analyzed for Pregabalin content using

standard techniques. Fig. 1 illustrates comparative dissolution profile of the chewable tablets of Pregabalin and Lyrica®

Example 5: Sensory Evaluation of Taste Masked Pregabalin tablets

Twenty-two panelists evaluated the composition specified in example 3 on sensory evaluation criteria for different attributes such as flavor, mouth feel and taste, where score 1 meant disliked extremely and score 9 meant liked extremely. The results are depicted in Table 4-6.

Table 4: Evaluation of flavour by Panelists

	Score	No. of Panelists	%	Comments
Flavour	3	1	5	-
	6	2	9	Ok
	7	10	45	Good / Increase slightly
	8	8	36	Good / Appropriate / Should be less
	9	1	5	Very good
Total Panelists		22	100	

Table 5: Evaluation of mouth feel effect by Panelist

	Score	No. of Panelists	%	Comments
Mouth feel	3	1	5	-
	4	1	5	Ok
	5	2	9	Good / Increase slightly
	6	6	27	
	7	9	41	
	8	2	9	Good / Appropriate / Should be less
	9	1	5	Very good
Total Panelists		22	100	

Table 6: Evaluation of taste by Panelists

	Score	No. of Panelists	%	Comments
Taste	3	2	9	Bitter
	4	1	5	Slight Bitter after 10 sec
	5	1	5	Increase sweetener slightly
	6	4	18	After taste Slight Bitter
	7	9	41	Good
	8	4	18	Very Good
	9	1	5	Excellent
Total Panelists		22	100	

Sensory Evaluation Criteria

Score	Observation	Score	Observation	Score	Observation
9	Liked extremely	6	Liked slightly	3	Disliked moderately
8	Liked very much	5	Neither liked nor disliked	2	Disliked very much
7	Liked moderately	4	Disliked slightly	1	Disliked extremely

We Claim:

1. A taste masked pharmaceutical composition of pregabalin or salts or enantiomers thereof, wherein the taste masking is achieved by using one or more of ion exchange resins, methacrylate polymers or cyclodextrins or derivatives thereof.

2. The taste masked pharmaceutical composition according to claim 1, wherein the ion exchange resin comprises an anion exchange resin or a cation exchange resin.

3. The taste masked pharmaceutical composition according to claim 2, wherein ion exchange resins is selected from one or more of polacrilex resin, polacrilin potassium, sodium polystyrene sulfonated or cholestyramine resin.

4. The taste masked pharmaceutical composition according to claim 1, wherein the methacrylate polymers comprises one or more of Eudragit E100 or Eudragit EPO.

5. The taste masked pharmaceutical composition according to claim 1, wherein composition comprises an inclusion complex of pregabalin or pharmaceutically acceptable salt with cyclodextrin or derivative thereof.

6. The taste masked pharmaceutical composition according to claim 1, wherein pharmaceutical composition comprises an admixture of pregabalin or pharmaceutically acceptable salt with cyclodextrin or derivative thereof.

7. The taste masked pharmaceutical composition according to claims 1, 5, and 6, wherein cyclodextrin or derivatives thereof are selected from the group consisting of α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, hydroxypropyl- α–cyclodextrin, hydroxypropyl-β-cyclodextrin, dimethyl – β- cyclodextrin, 2-hydroxyethyl β – cyclodextrin, trimethyl -β –cyclodextrin, and sulfonated cyclodextrins, in anhydrous or hydrated form.

8. The taste masked pharmaceutical composition according to claim 1, further comprising one or more of pharmaceutically acceptable excipients selected from the group consisting of binders, fillers, disintegrants, glidants, lubricants, surfactants, sweeteners and flavors.

9. The taste masked pharmaceutical composition according to any of the preceeding claims, wherein the dosage form is a tablet, capsule, powder, disc, caplet, granules, pellets, granules in capsule, minitablets, minitablets in capsule, pellets in capsule, sachet, orally disintegrating tablet, chewable tablet, effervescent tablet, mouth dissolving film, syrup, solution, suspension, elixir, emulsion and other dosage forms suitable for oral administration.

10. The taste masked pharmaceutical composition according to claim 9, wherein the composition is an orally disintegrating tablet.

11. The taste masked pharmaceutical composition according to claim 9, wherein the composition is a chewable tablet.

12. A quick release pharmaceutical composition comprising pregabalin or salts or enantiomers thereof, wherein the composition releases not less than about 60% of the dose in 30 minutes when tested for dissolution using United States Pharmacopoeia Apparatus 2 (paddles@ 50 rpm in 900 mL of 0.06 N HCl).

13. The quick release pharmaceutical composition according to claim 12, wherein the composition is taste masked.

14. The quick release pharmaceutical composition according to claim 13, wherein taste masking is achieved by using one or more of ion exchange resins, methacrylate polymers or cyclodextrins or derivatives thereof.

15. The quick release pharmaceutical composition according to claim 14, wherein the ion exchange resin comprises an anion exchange resin or a cation exchange resin.

16. The quick release pharmaceutical composition according to claim 13, wherein the methacrylate polymers comprises one or more of Eudragit E100 or Eudragit EPO.

17. The quick release pharmaceutical composition according to claim 13, wherein cyclodextrin or derivatives thereof are selected from the group consisting of α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, hydroxypropyl- α–cyclodextrin, hydroxypropyl-β-cyclodextrin, dimethyl – β- cyclodextrin, 2-hydroxyethyl β – cyclodextrin, trimethyl -β –cyclodextrin, and sulfonated cyclodextrins, in anhydrous or hydrated form.

18. The quick release pharmaceutical composition according claims 12-17, further comprising one or more of pharmaceutically acceptable excipients selected from the group consisting of binders, fillers, disintegrants, glidants, lubricants, surfactants, sweeteners and flavors.

19. The quick release pharmaceutical composition according to claims 12-18, can be a tablet, capsule, powder, disc, caplet, granules, pellets, granules in capsule, minitablets, minitablets in capsule, pellets in capsule, sachet, orally disintegrating tablet, chewable tablet, effervescent tablet, mouth dissolving film, syrup, solution, suspension, elixir, emulsion and other dosage forms suitable for oral administration.

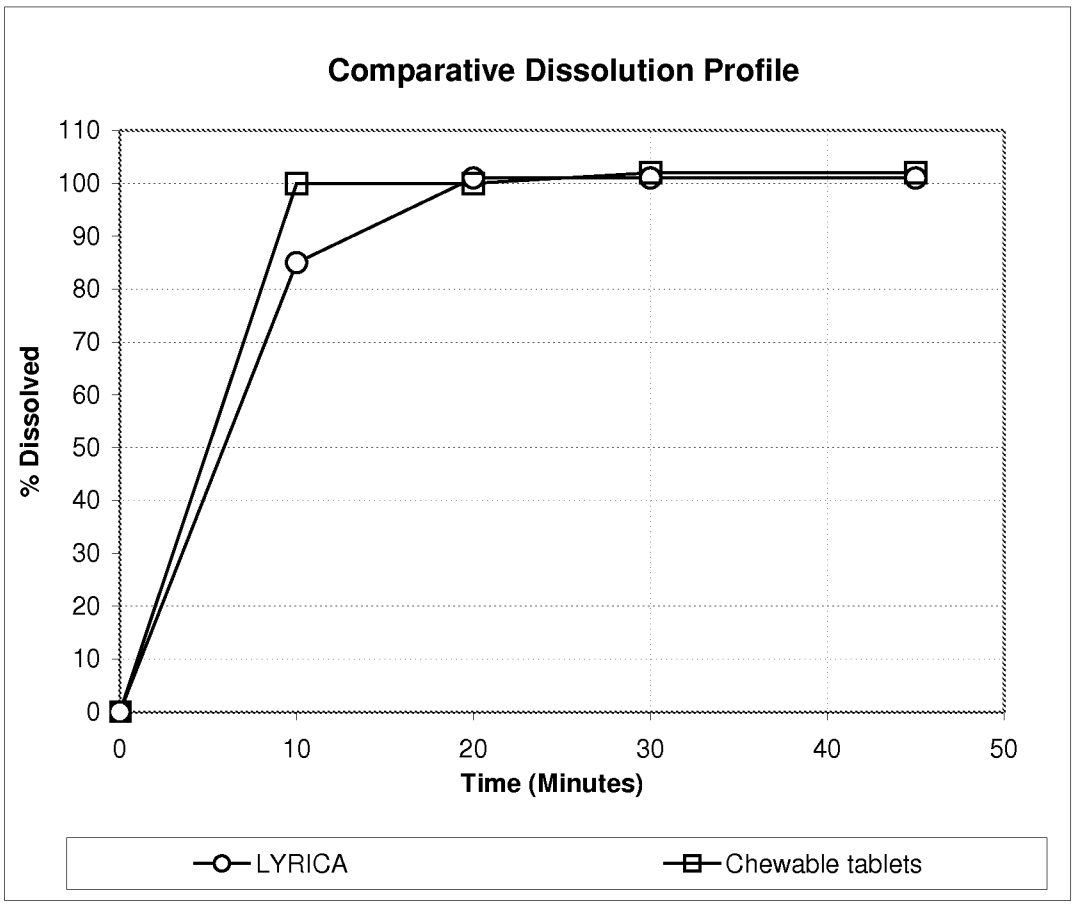
20. The quick release pharmaceutical composition according to claims 19, wherein the quick release composition is an orally disintegrating tablet.

21. The orally disintegrating tablet according to claim 20, wherein the hardness of the tablet is in the range of about 15 Newtons to about 70 Newtons.

22. The quick release pharmaceutical composition according to claims 19, wherein the quick release composition is a chewable tablet.

23. The quick release pharmaceutical composition according to claim 12, wherein the composition releases not less than about 80% of the dose in 30 minutes when tested for dissolution using United States Pharmacopoeia Apparatus 2 (paddles@ 50 rpm in 900 mL of 0.06 N HCl).

FIGURE 1: COMPARATIVE DISSOLUTION PROFILE OF PREGABALIN CHEWABLE TABLETS AND LYRICA®



INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2010/052885

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/00 A61K9/20 A61K31/195
ADD.

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

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 488 964 B2 (BRUNA ETIENNE [FR] ET AL) 3 December 2002 (2002-12-03) cited in the application the whole document	1-23
X	US 2006/182796 A1 (WU CHUANBIN [US] ET AL) 17 August 2006 (2006-08-17) the whole document paragraph [0050]	1-23
X	US 6 660 382 B2 (NOURI NOUREDDINE [FR] ET AL NOURI NOUREDDINE [FR] ET AL) 9 December 2003 (2003-12-09) cited in the application column 3, line 17 - column 3, line 52; figure 3; example 3	1-23

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
18 October 2010	08/11/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Sproll, Susanne

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2010/052885

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SIOK C J ET AL: "Anxiolytic profile of pregabalin on elicited hippocampal theta oscillation" NEUROPHARMACOLOGY, PERGAMON PRESS, OXFORD, GB LNKD- DOI:10.1016/J.NEUROPHARM.2008.09.013, vol. 56, no. 2, 1 February 2009 (2009-02-01), pages 379-385, XP025914031 ISSN: 0028-3908 [retrieved on 2009-02-01] Chapter under heading "2.4. Drugs"	1-23
Y	US 2008/003296 A1 (KETNER RODNEY J [US]) 3 January 2008 (2008-01-03) paragraph [0043]	1-11
X	US 2007/092553 A1 (TENGLER MARK [US] ET AL) 26 April 2007 (2007-04-26) * abstract examples; paragraphs [0001], [0010], [0038], [0107]	1-23
X	WO 2006/008640 A1 (PHARMACIA & UPJOHN CO LLC [US]; PENA LORRAINE ELISABETH [US]) 26 January 2006 (2006-01-26)	12-23
Y	* abstract; example 4	1-11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2010/052885

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6488964 B2	03-12-2002	AU 742701 B2	10-01-2002
		AU 4916099 A	28-02-2000
		CA 2338173 A1	17-02-2000
		CN 1321083 A	07-11-2001
		EP 1100467 A1	23-05-2001
		FR 2781793 A1	04-02-2000
		WO 0007568 A1	17-02-2000
		JP 2002522375 T	23-07-2002
		NZ 509980 A	25-07-2003
		US 2002012679 A1	31-01-2002
		ZA 200100943 A	05-09-2001
US 2006182796 A1	17-08-2006	NONE	
US 6660382 B2	09-12-2003	AT 360412 T	15-05-2007
		AU 760006 B2	08-05-2003
		AU 5993600 A	30-01-2001
		BG 65615 B1	31-03-2009
		BG 106398 A	30-09-2002
		BR 0012250 A	26-03-2002
		CA 2375600 A1	18-01-2001
		CN 1373658 A	09-10-2002
		CZ 20020018 A3	17-04-2002
		DE 60034565 T2	27-12-2007
		DK 1194125 T3	30-07-2007
		EP 1194125 A1	10-04-2002
		ES 2284507 T3	16-11-2007
		WO 0103672 A1	18-01-2001
		FR 2795962 A1	12-01-2001
		HK 1049119 A1	12-05-2006
		HU 0202062 A2	28-12-2002
		IL 147212 A	15-05-2007
		JP 2003504324 T	04-02-2003
		MA 25426 A1	01-04-2002
		MX PA01013354 A	09-07-2002
		NO 20016308 A	21-12-2001
		NZ 516594 A	28-11-2003
		PL 354257 A1	29-12-2003
		PT 1194125 E	03-07-2007
		SK 19392001 A3	04-04-2002
		TR 200200013 T2	21-06-2002
		US 2002098227 A1	25-07-2002
		ZA 200200344 A	26-03-2003
US 2008003296 A1	03-01-2008	NONE	
US 2007092553 A1	26-04-2007	NONE	
WO 2006008640 A1	26-01-2006	NONE	