The examination is being carried out on the following application documents:

#### **Description, Pages**

1-50

as published

#### Claims, Numbers

1-30

filed with entry into the regional phase before the EPO

- 1. The present application refers to the use of a Withania somnifera plant extract for the preparation of a composition for treating or managing stress disorders.
- 2. Reference is made to the following documents; the numbering will be adhered to in the rest of the procedure:
  - D1: US-B1-6 713 092
  - D2: BHATTACHARYA S K ET AL: "Antioxidant activity of glycowithanolides from withania somnifera" INDIAN JOURNAL OF EXPERIMENTAL BIOLOGY, COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH, IN, vol. 35, no. 3, 1 March 1997 (1997-03-01), pages 236-239.
  - D3: BHATTACHARYA S K ET AL: "Anxiolytic-antidepressant activity of Withania somnifera glycowithanolides: An experimental study" PHYTOMEDICINE (JENA), vol. 7, no. 6, December 2000 (2000-12), pages 463-469.
  - D4: BHATTACHARYA S K ET AL: "Adaptogenic activity of Withania somnifera: An experimental study using a rat model of chronic stress." PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR, vol. 75, no. 3, June 2003 (2003-06), pages 547-555.
  - D5: JAIN S ET AL: "Neuroprotective effects of Withania somnifera Dunn. in hippocampal sub-regions of female albino rat." PHYTOTHERAPY RESEARCH: PTR SEP 2001, vol. 15, no. 6, September 2001 (2001-09), pages 544-548.

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D6: "Withania somnifera" ALTERNATIVE MEDICINE REVIEW 200406 US, vol. 9, no. 2, June 2004 (2004-06), pages 211-214.

- D7: MISHRA L C ET AL: "Scientific basis for the therapeutic use of Withania somnifera (ashwagandha): a review." ALTERNATIVE MEDICINE REVIEW: A JOURNAL OF CLINICAL THERAPEUTIC AUG 2000, vol. 5, no. 4, August 2000 (2000-08), pages 334-346.
- D8: ARCHANA R ET AL: "Antistressor effect of Withania somnifera" JOURNAL OF ETHNOPHARMACOLOGY, vol. 64, no. 1, January 1999 (1999-01), pages 91-93.
- D9: BHATNAGAR MAHEEP ET AL: "Antiulcer and antioxidant activity of Asparagus racemosus Willd and Withania somnifera Dunal in rats." ANNALS OF THE NEW YORK ACADEMY OF SCIENCES NOV 2005, vol. 1056, November 2005 (2005-11), pages 261-278.
- D10: DATABASE TKDL "Asvagandhadi Yoga" retrieved from TKDL Database accession no. AK11/4074
- D11: DATABASE TKDL "Asvagandhadi Curna" retrieved from TKDL Database accession no. RG12/1062
- D12: DATABASE TKDL "Parangi Chooranam 7" retrieved from TKDL Database accession no. AM05/1804
- D13: DATABASE TKDL "Aswaganthathy Chooranum" retrieved from TKDL Database accession no. SP01/75
- D14: DATABASE TKDL "Vaayu Thiratchiku Mezhugu" retrieved from TKDL Database accession no. AM05/1838
- D15: DATABASE TKDL "Safoof -e- Asgandh 1" retrieved from TKDL Database accession no. NA2/108V
- D16: DATABASE TKDL "Amukkara Karpam" retrieved from TKDL Database accession no. PD04/54
- D17: DATABASE TKDL "Phalasava" retrieved from TKDL Database accession no. RS21/797

#### 3. Novelty; Article 54 EPC.

3.1 The document D1 discloses high purity Withania somnifera extracts comprising withanolide glycosides, oligosaccharides and withanolide aglycones (Abstract). Said extracts have application as adaptogen or antistress agent (column 4, line 45 to column 7, line 35). The compositions of D1 can be in the form of lotions (examples 1, 3, 4 and 5), creams (example 2), tablets and capsules (examples 6, 7, 8, 9 and 10), beverages (example 11)

or cereals (example 12).

In the light of this document, the subject-matter of claims 1-10, 12-26 and 28-29 cannot be considered as novel (Article 54 EPC).

3.2 The document D2 discloses the antioxidant activity of sitoindoside VII-X and withaferin A of Withania somnifera. According to the authors of D2, these antioxidant principles may explain the anti-stress effect of Withania somnifera (Abstract). D2 also points out that sitoindosides VII to X and withaferin A have been shown to induce significant antistress effects (p. 236, paragraph bridging the two columns). The active principles have been obtained by chloroform extraction of an aqueous concentrate of W. somnifera roots (p. 237, left-hand column, lines 15-18). The Search Authority considers that the extract will comprise withanolide glycosides, oligosaccharides and withanolide aglycones.

Therefore, the subject-matter of claims 1-4, 6-7, 12-18, 20-23, 25 and 28 cannot be considered as novel over the teaching of D2 (Article 54 EPC).

3.3 The document D3 discloses the anxiolytic-antidepressant activity of Withania somnifera glycowithanolides administered to rats daily for 5 days at dosage of 20 and 50 mg/kg. Said glycowithanolides exhibit an antidepressant effect comparable with that induced by imipramine (Abstract). D3 mentions that sitoindosides VII to X and withaferin A have previously been found to prevent acute stress-induced anxiety and chronic stress induced depression (p. 463, left-hand column, line 12 to right-hand column, line 5). The glycowithanolides used in D3 have been obtained by extracting an aqueous concentrate of WS roots with chloroform to remove fatty materials and free withanolides (p. 464, left-hand column, lines 15-21). The Search Authority considers that these extracts comprise withanolide glycosides, oligosaccharides and withanolides aglycones.

In the light of this document, the subject-matter of claims 1-4, 6-7, 10-23, 25 and 28 cannot be considered as novel in the sense of Article 54 EPC.

3.4 D4 discloses studies on the adaptogenic activity of a standardised extract of WS roots against a rat model of chronic stress. The WS extract was shown to attenuate the effects of hyperglycaemia, glucose intolerance, increase

plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficit, immunosuppression and mental depression. According to the authors of D4, WS has significant antistress adaptogenic activity (Abstract). D4 also mentions the fact that the active principles of WS comprising sitoindosides VII to X and withaferin A were show to have significant antistress activity against acute models of experimental stress (p. 547, right-hand column, lines 3-18). The WS extracts used in D4 have been obtained by extraction of WS roots with aqueous ethanol followed by chloroform extraction to remove fatty material and free withanolides (p. 548, right-hand column: 2.1 Plant material). The WS extract used in D4 are considered to comprise withanolide glycosides, oligosaccharides and withanolide aglycones.

The subject-matter of claims 1-4, 6-7, 10-23, 25 and 28 cannot be considered as novel over the teaching of D4 (Article 54 EPC).

- 3.5 The document D5 discloses the antistress neuroprotective effect of Withania somnifera root powder extract (Abstract). The W. somnifera extract is a hydroalcoholic extract standardized for withanolides. This extract was administered together with soya lectins, bees wax and arachis oil (p. 544, right-hand column: Drug preparation). D5 concludes that the WS extract has a cytoprotective antistress effect on hippocampal cell bodies. The Search Authority considers that the WS extract disclosed in D5 comprises withanolide glycosides, oligosaccharides and withanolide aglycones.
  - In the light of this document, the subject-matter of claims 1-7, 9, 11, 13-18, 20, 22-23, 25-26 and 28-29 cannot be considered as novel (Article 54 EPC).
- 3.6 The document D6 discloses the therapeutic effects of Withania somnifera. In said document, it is mentioned that WS extract exhibits anti-depressant, anxiolytic and anti-stress activities (p. 212-213). The active constituents of W. somnifera roots include withanolides (p. 211 : Active Constituents). The Search Authority considers that WS root extracts will comprise withanolide glycosides, oligosaccharides and withanolide aglycones.

In the light of this document, the subject-matter of claims 1-4, 6-7, 11 and 13-17 lacks novelty (Article 54 EPC).

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- Document D7 discloses, inter alia, the anti-stress properties of Withania somnifera in numerous types of stress (Abstract; p. 338-339 : Antistress Effect). The extracts of D7 are considered to comprise with anolide glycosides, oligosaccharides and withanolides aglycones.
  - Therefore, the subject-matter of claims 1-4, 6-7, 11-17, 20-23, 25 and 28 cannot be considered as novel over the teaching of D7 (Article 54 EPC).
- The document D8 discloses the antistressor properties of Withania somnifera in a cold water swimming stress test (Abstract). The WS extract used in D8 is powdered root of W. somnifera in aqueous suspension and used at a dosage of 100 mg/kg (p. 92, left-hand column: first paragraph of Material and methods). D8 concludes that W. somnifera root extract is a potent antistressor agent (p. 93, lines 14-17). The extracts of D8 are considered to comprise withanolide glycosides, oligosaccharides and withanolides aglycones.
  - Therefore, claims 1-4, 6-9, 12-23, 25 and 28 cannot be considered as novel over the teaching of D8 (Article 54 EPC).
- 3.9 The document D9 discloses the fact that a methanolic extract of Withania somnifera was able to reduce stress-induced gastric ulcers (Abstract). Gastric ulcers were induced inter alia by restraint swim test (p. 262 : Material and Methods: Treatment). The Search Authority considers that the methanolic extract of W. somnifera will contain withanolide glycosides, oligosaccharides and withanolide aglycones.
  - Therefore, the subject-matter of claims 1-4, 6-7, 11, 13-23, 25 and 28 cannot be considered as novel over the teaching of D9 (Article 54 EPC).
- 3.10 The document D10 is an entry of the Traditional Knowledge Digital Library which refers to a composition comprising Withania somnifera root powder, a product of sugarcane and clarified butter. This composition is useful for the treatment of insomnia.
  - The Search Authority considers that the Withania somnifera extract used in this composition will comprise withanolide glycosides, oligosaccharides and withanolide aglycones since this compounds are naturally present in Withania somnifera roots.

Insomnia is considered to be a chronic stress disorder.

Clarified butter is considered to comprise fatty acids and vitamins.

In the light of this document, the subject-matter of claims 1-4, 6-7, 10-11, 13-17, 20-26, 28 and 29 cannot be considered as novel (Article 54 EPC).

3.11 The document D11 is an entry of the Traditional Knowledge Digital Library which discloses a therapeutic composition for the treatment of insomnia which comprises a root extract from Withania somnifera and a root extract from Argyeria nervosa (a plant extract). Said composition can be administered together with milk or water and is thus considered to fulfil the definition of a beverage.

The Search Authority considers that the Withania somnifera extract used in this composition will comprise withanolide glycosides, oligosaccharides and withanolide aglycones since this compounds are naturally present in Withania somnifera roots.

Insomnia is considered to be a chronic stress disorder.

In the light of D11, the subject-matter of claims 1-4, 6-11, 13-17, 20-26, 28 and 29 cannot be considered as novel in the sense of Article 54 EPC.

3.12 Documents D12, D13 and D16 are entries of the Traditional Knowledge Digital Library which disclose therapeutic compositions comprising a Withania somnifera root extract together with other plant extracts for the treatment of gastric ulcers or acute gastritis. The composition is in the form of a powder.

The Search Authority considers that the Withania somnifera extract used in these compositions will comprise withanolide glycosides, oligosaccharides and withanolide aglycones since this compounds are naturally present in Withania somnifera roots.

Gastric ulcers are considered to be chronic stress disorders.

Therefore, the subject-matter of claims 1-4, 6-7, 11-17, 20-26, 28 and 29 cannot be considered as novel (Article 54 EPC).

3.13 The document D14 is an entry of the Traditional Knowledge Digital Library which discloses a therapeutic composition for the treatment of gastric ulcers and acute gastritis comprising numerous plant extracts. One of these

extracts is a Withania somnifera root extract. The composition further comprises garlic extracts. The composition is waxy.

The Search Authority considers that the Withania somnifera extract used in this composition will comprise withanolide glycosides, oligosaccharides and withanolide aglycones since this compounds are naturally present in Withania somnifera roots.

Gastric ulcers are considered to be chronic stress disorders.

Therefore, the subject-matter of claims 1-4, 6-7, 11-17 and 20-30 cannot be considered as novel (Article 54 EPC).

3.14 The document D15 is an entry of the Traditional Knowledge Digital Library which discloses a therapeutic composition for the treatment of restlessness and depression comprising Withania somnifera bark, leaf, flower, fruit and root extracts, Terminalia bellirica root extract and a sugar cane product. The composition is formulated as a powder.

The Search Authority considers that the Withania somnifera extract used in this composition will comprise withanolide glycosides, oligosaccharides and withanolide aglycones since this compounds are naturally present in Withania somnifera roots.

Restlessness and depression are considered to be chronic stress disorders.

Therefore, the subject-matter of claims 1-4, 6-7, 10-11, 13-17, 20-26, 28 and 29 cannot be considered as novel over the teaching of D15 (Article 54 EPC).

3.15 The document D17 is an entry of the Traditional Knowledge Digital Library which discloses a therapeutic composition for the treatment of hyperacidity and insomnia comprising numerous plant extracts including a Withania somnifera root extract. The composition is in the form of a fermented alcoholic product and fulfil the definition of a beverage or elixir.

The Search Authority considers that the Withania somnifera extract used in this composition will comprise withanolide glycosides, oligosaccharides and withanolide aglycones since this compounds are naturally present in Withania somnifera roots.

Hyperacidity and insomnia are considered to be chronic stress disorders.

Therefore, the subject-matter of claims 1-11, 13-17, 20-26, 28 and 29 cannot be considered as novel over the teaching of D17 (Article 54 EPC).

#### 4. Clarity; Article 84 EPC.

- 4.1 Claim 1 of the present application lacks clarity for the following reasons:
  - (i) Claim 1 refers to a Withania somnifera plant extract. It is not clear what should be the composition of such an extract or how it should be produced, what renders the scope of the claim unclear. In the present opinion, any part of Withania somnifera has been considered as a plant extract.
    - This remark also applies mutatis mutandis to claims 27 and 30.
  - (ii) It is not clear what a "stress disorder" should precisely mean.
  - (iii) Claim 1 refers to the step of "managing stress disorders". It is not clear what this wording should precisely mean.
- 4.2 Claim 2 refers to several stresses to be treated with the compositions of the present application. It is not clear for the Search Authority what these stresses should precisely be and how to distinguish these different kind of stresses.

This remark also applies to claims 15 and 16.

- 4.3 Claim 3 states that the Withania somnifera plant extract should comprise withanolide glycosides, oligosaccharides and withanolide aglycones. However, it is not clear in which proportions these compounds should be present in the extract what renders the scope of the claim unclear.
- 4.4 Claim 4 refers to pharmaceutically, veterinary or nutritionally acceptable carriers. It is not clear what such carriers should precisely be what renders the scope of the claim unclear.

This remark also applies to claims 6 and 7.

- 4.5 In claim 5, it is not clear what an "elixir" should precisely be.
- 4.6 In claim 10, the composition should provide improvement in various disorders. It is not clear what "provide improvement" should precisely mean in relation with the various disorders.
- 4.7 Claim 13 states that the composition provides reduction in fasting sugar,

cholesterol, triglycerides low-density lipids, C-reactive proteins and cortisol. The Search Authority considers that these effects are automatically achieved by all the Withania somnifera extracts which have been used to treat stress disorders. If this is not the case, the Applicant is invited to indicate how these effects should be achieved in terms of technical characteristics of the composition.

This remark also applies mutatis mutandis to claims 14 and 17.

4.8 Claim 18 is drafted in the form of a second medical use claim. However, claim 18 further states that the composition is administered (to a patient). Therefore, it is not clear if claim 18 should be considered as a second medical use claim or rather a claim directed to a method of treatment.

This remark also applies to claims 19-30.

4.9 Claim 24 refers to a general "active ingredient". It is not clear what such an ingredient should precisely be, what renders the scope of the claim unclear.



	DOCUMENTS CONSIDER		1	
Category	Citation of document with indica of relevant passages		Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	BHATTACHARYA S K ET A activity of glycowith withania somnifera" INDIAN JOURNAL OF EXPLOUNCIL OF SCIENTIFIC RESEARCH, IN, vol. 35, no. 3, 1 Marchages 236-239, XP00299 ISSN: 0019-5189 * abstract * * page 236, left-hand right-hand column, line 18 * * page 239, left-hand line 24 *	enolides from ERIMENTAL BIOLOGY, AND INDUSTRIAL  ch 1997 (1997-03-01), 58783  column, line 23 - ne 3 * column, line 15 -	1-30	INV. A61K36/00
X	BHATTACHARYA S K ET A "Anxiolytic-antidepre: Withania somnifera gly experimental study" PHYTOMEDICINE (JENA), vol. 7, no. 6, December pages 463-469, XP00912 ISSN: 0944-7113 * abstract * * page 463, left-hand right-hand column, line 21 * * page 464, left-hand line 21 * * page 468, left-hand right-hand column, line 18 *	er 2000 (2000-12), 23940  column, line 12 - ne 5 * column, line 15 - column, line 34 - ne 14 * column, line 12 -	1-30	TECHNICAL FIELDS SEARCHED (IPC) A61K
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X	BHATTACHARYA S K ET AL activity of Withania s experimental study using chronic stress." PHARMACOLOGY BIOCHEMIS vol. 75, no. 3, June 2547-555, XP002549684 ISSN: 0091-3057 * abstract * * page 547, right-handline 18 * * page 548, right-handline 28 * * page 552, right-handline 33 *	somnifera: Ån ng a rat model of GTRY AND BEHAVIOR, 2003 (2003-06), pages d column, line 3 -	1-30	
X	JAIN S ET AL: "Neurop Withania somnifera Dur sub-regions of female PHYTOTHERAPY RESEARCH vol. 15, no. 6, Septen pages 544-548, XP00254 ISSN: 0951-418X * abstract * * page 547, right-hand line 14 * * page 547, right-hand	nn. in hippocampal albino rat." : PTR SEP 2001, nber 2001 (2001-09), 19685	1-30	TECHNICAL FIELDS SEARCHED (IPC)
X	"Withania somnifera' ALTERNATIVE MEDICINE F vol. 9, no. 2, June 26 211-214, XP002549686 ISSN: 1089-5159 * abstract * * page 213, left-hand line 23 *  The supplementary search report has set of claims valid and available at the	REVIEW 200406 US, 1004 (2004-06), pages column, line 16 -	1-30	
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	DOCUMENTS CONSID	ERED TO BE RELEVANT		
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X	the therapeutic use (ashwagandha): a re ALTERNATIVE MEDICIN CLINICAL THERAPEUTI vol. 5, no. 4, Augu pages 334-346, XP06 ISSN: 1089-5159 * abstract *	IE REVIEW: A JOURNAL OF C AUG 2000, est 2000 (2000-08), e2549687	1-30	
X	Withania somnifera" JOURNAL OF ETHNOPHA vol. 64, no. 1, Jar pages 91-93, XP0025 ISSN: 0378-8741 * abstract * * page 92, left-har line 20 *	RMACOLOGY, nuary 1999 (1999-01),	1-30	TECHNICAL FIELDS SEARCHED (IPC)
X	antioxidant activit racemosus Willd and Dunal in rats." ANNALS OF THE NEW Y NOV 2005, vol. 1056, November 261-278, XP00254968 ISSN: 0077-8923 * abstract *	Withania somnifera  ORK ACADEMY OF SCIENCES  2005 (2005-11), pages	1-30	
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X	DATABASE TKDL "Phal XP002549697 retrieved from TKDL Database accession * abstract *		797	1-29	26,28,		
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