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(71) Applicant *(for all designated States except US)*: **IOMEDIX DEVELOPMENT INTERNATIONAL SRL** [CA/CA]; The Grove, 21 Pine Road, Belleville,, St. Michael, BB11113 (BB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **HEUER, Marvin** [US/CA]; 381 North Service Road West, Oakville, Ontario L6M 0H4 (CA). **CLEMENT, Ken** [CA/CA]; 381 North Service Road West, Oakville, Ontario L6M 0H4 (CA). **CHAUDHURI, Shan** [CA/CA]; 1 Castle Mountain Drive, Brampton, Ontario L6R 2Y1 (CA). **THOMAS, Megan** [CA/CA]; 381 North Service Road West, Oakville, Ontario L6M 0H4 (CA).

(74) Agent: **TORYS LLP**; 79 Wellington Street West, Suite 3000, Box 270, TD Centre, Toronto, Ontario M5K 1N2 (CA).

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(54) Title: COMPOSITION FOR SUPPORTING RESTFUL SLEEP COMPRISING VALERIAN ROOT EXTRACT AND METHYLCOBALAMIM

(57) Abstract: A method for promoting and supporting restful, quality sleep in an individual comprising the administration of a composition comprising Valerian root extract and Methylcobalamin.

Composition for supporting restful sleep comprising Valerian root extract and Methylcobalamin.

Field of the Invention

[001] The present invention relates to supplemental compositions and methods for promoting and supporting restful sleep in an individual via the induction of sedation and melatonin support.

Background of the Invention

[002] Sleep occupies about one-third of our life and is necessary for mental and physical well-being. It additionally affects mood, behavior and physiology. The need for sleep is a biological drive similar to thirst or hunger. Interestingly though, the function of sleep is largely unknown, however some evidence indicates that sleep is required for learning. It is clear that the impairment of sleep is detrimental to one's health. In humans, similarly, mild sleep deprivation also results in indications of impaired immune system function (Irwin M, McClintick J, Costlow C, Fortner M, White J, Gillin JC. Partial night sleep deprivation reduces natural killer and cellular immune responses in humans. FASEB J. 1996 Apr;10(5):643-53.). Prolonged sleep deprivation is even known to result in death. It has been determined my many that an individual can survive longer without food than one can without sleep; thus indicating the importance of sleep. Additionally, insomnia is estimated to affect a significant portion of North Americans per year and is associated with health problems and economic loss (Stoller MK. Economic effects of insomnia. Clin Ther. 1994 Sep-Oct;16(5):873-97 Abstract).

[003] Sleep as well as the control of sleep are complex processes involving multiple neuro-chemical pathways and associated brain structures. It is a shift in the balance of distinct physiological changes, involving bothe distinct physiological changes and involves both positive and negative neural signaling.. The regulation of sleep in humans is governed by three processes – each influenced by hormonal and environmental factors: a daily sleep-wake cycle influenced by a circadian rhythm (24 hour cycle) tied to light-dark cycles.

[004] Strategies to improve sleep are beneficial, not only in terms of physical health, but also in terms of emotional health. Furthermore, reinforcement of sleep of adequate quantity and quality positively impacts most aspect of daily life.

Summary of the Invention

[005] The foregoing needs and other needs and objectives that will become apparent for the following description are achieved in the present invention, which comprises Valerian root extract and Methylcobalamin for the support of restful sleep in an individual via the induction of sedation and providing anxiolytic compounds and melatonin support.

Detailed Description of the Invention

[006] In the following description, for the purposes of explanations, numerous specific details are set forth in order to provide a thorough understanding of the present invention. It will be apparent, however, to one of ordinary skill in the art that the present invention may be practiced without these specific details.

[007] The present invention is directed towards a composition for supporting a restful period of sleep via the induction of sedation and providing anxiolytic compounds comprising Valerian root extract and Methylcobalamin. A method for same also provided comprising the step of the administration to an individual a composition comprising an extract of Valerian root supplying valerinic acid and Methlycobalamin.

[008] Incorporated herein by reference are the specifications of co-pending applications (filed contemporaneously with the present application) entitled "Composition for a Feeling of Relaxation" and "Composition for a Feeling of Calmness".

[009] It is herein understood that improvements in sleep may be both of a quantitative nature e.g. increased length of sleep, decreased time of sleep onset, and of a qualitative nature e.g. deeper, more restful undisturbed. It is further understood that improvements in sleep may also be both direct and indirect. For example, sleep will be directly improved by the administration of a substance which is known to reduce time to sleep onset. Sleep may be indirectly improved, for example, by the administration of a substance which is known to result in feelings of relaxation and calmness.

Valerian Root Extract

[0010] Valerian (*Valeriana officinalis*) is a perennial plant native to North America, Asia and Europe. The root has been traditionally used as treatment for anxiety and insomnia. A meta-analysis of available studies suggest that Valerian root extract may improve sleep absent of side-effects (Bent S, Padula A, Moore D, Patterson M, Mehling W. Valerian for sleep: a systematic review and meta-analysis. Am J Med. 2006 Dec;119(12):1005-12 Abstract) acting particularly to decrease the time to sleep onset and improved sleep quality in individuals.

[0011] Valerian has been shown to modulate Gamma Aminobutyric Acid (GABA) receptors (Yuan CS, Mehendale S, Xiao Y, Aung HH, Xie JT, Ang-Lee MK. The gamma-aminobutyric acidergic effects of valerian and valerenic acid on rat brainstem neuronal activity. Anesth Analg. 2004 Feb;98(2):353-8). The neurotransmitter GABA, is the primary inhibitory neurotransmitter of the Central Nervous system. One of its effects is to induce sleep. Signaling through the GABA-receptor changes the electrochemical gradient of a given neuron, leading to inhibition of its activity. Benzodiazepines are thought to act via interaction with the GABA receptor; enhancing the inhibitory effects of GABA. As such, benzodiazepines are a widely used class of drugs primarily used as tranquilizers, muscle-relaxants, hypnotics or sedatives. It is believed that active constituents of Valerian produce sleep-enhancing sedative effects through this mechanism (Hadley S, Petry JJ. Valerian. Am Fam Physician. 2003 Apr 15;67(8):1755-8).

[0012] Valerinic acid specifically has been shown to decrease neural activity in the brainstem produced by the GABA receptor antagonist, muscimol. Data from this study suggests that the pharmacological effects of valerian extract and valerenic acid are mediated through modulation of GABA(A) receptor function (Yuan CS, Mehendale S, Xiao Y, Aung HH, Xie JT, Ang-Lee MK. The gamma-aminobutyric acidergic effects of valerian and valerenic acid on rat brainstem neuronal activity. Anesth Analg. 2004 Feb;98(2):353-8).

[0013] In a preferred embodiment of the present invention which is set forth in greater detail in the example below, the composition includes an extract of Valerian root having valerinic acid as an active component to promote a sedation leading to sleep through a GABAergic-dependant mechanism. A serving of the supplemental

composition includes from about 0.001 g to about 1.000 g of an extract of Valerian root. The preferred dosage of an extract of Valerian root in the present invention comprises about 0.100 g per serving.

Vitamin B12 (Methylcobalamin)

[0014] Vitamin B12 is a water-soluble cofactor for the enzyme methionine synthase, which transfers methyl groups. There are two forms of Vitamin B12 – Adenosylcobalamin which is usually present in tissue and Methylcobalamin which is usually present in plasma. Vitamin B12 plays an important role in many important biological processes (Volkov I, Press Y, Rudoy I. Vitamin B12 could be a "master key" in the regulation of multiple pathological processes. J Nippon Med Sch. 2006 Apr;73(2):65-9).

[0015] One specific area of vitamin B12 research pertains to the treatment of sleep disturbances. The Methylcobalamin form of vitamin B12 has been shown to be associated with increases in the quality of sleep and feelings of post-sleep restfulness (Mayer G, Kroger M, Meier-Ewert K. Effects of vitamin B12 on performance and circadian rhythm in normal subjects. Neuropsychopharmacology. 1996 Nov;15(5):456-64). The mode of action of the benefit of vitamin B12 to sleep may be via support of melatonin synthesis (Methylcobalamin. Altern Med Rev. 1998 Dec;3(6):461-3).

[0016] Methylcobalamin, as noted above, plays a role in melatonin production. Melatonin is the hormone responsible for the proper cycling of normal diurnal rhythms, or the circadian rhythm. As people get older, the body is less efficient at making this hormone. B12 supplementation has been shown to help some older adults sleep better, most likely through an increase in melatonin production.

[0017] In a preferred embodiment of the present invention which is set forth in greater detail in the example below, the composition includes Methylcobalamin to promote quality sleep by supporting the endogenous function of melatonin. A serving of the supplemental composition includes from about 0.000001 g to about 0.00001 g of Methylcobalamin. The preferred dosage of Methylcobalamin in the present invention comprises about 0.000006 g per serving.

[0018] In a preferred embodiment of the present invention, the composition comprises an extract of Valerian root and Methylcobalamin for the support of a restful

period of sleep in an individual via the induction of sedation and melatonin support to maintain circadian rhythms relative to local time of a 24-hour day.

[0019] Not wishing to be bound by theory, it is believed that the components of the present invention will act in concert through distinct mechanisms to promote and support a restful period of sleep. The extract of Valerian root will act to promote sleep through the modulation GABA-receptors providing sedative and anxiolytic effect through GABA receptor agonism, while Methylcobalamin will act to support the normal endogenous activity of melatonin to regulate sleep according to a 24-hours system.

[0020] The composition of the present invention may be provided in various embodiments, however, the nutritional supplement resultant therefrom said embodiements may be administered to an individual in acceptable any form. For instance, the dosage form of the nutritional supplement may be provided as, e.g., a powder beverage mix, a liquid beverage, a ready-to-eat bar or drink product, a capsule, a liquid capsule, a tablet, a caplet, a soft-gel capsule or as a dietary gel. The preferred dosage forms of the present invention are as a tablet or caplet.

[0021] An embodiment of the present invention the composition may be provided in a solid dosage form having specific controlled release characteristics. Advantageously, the composition may be provided in a layered solid dosage form. In such a form, each individual layer will provide unique dissolution characteristics. In this way a controlled release of the composition can be achieved. In one aspect of this embodiment, each layer contains a homogeneous mixture of ingredients whereby the release of all ingredients is dependent upon the characteristics of each given layer. In an alternative aspect of this embodiment, each layer contains a distinct set of specific ingredients which differ according to the layers such that different specific ingredients are released from the solid dosage form at different times according to a predetermined schedule. In all aspects of this embodiment, a temporally controlled release of ingredients is achieved.

[0022] Furthermore, the dosage form of the nutritional supplement may be provided in accordance with customary processing techniques for herbal and nutritional supplements in any of the forms mentioned above. Additionally, the

nutritional supplement set forth in the example embodiment herein may contain any appropriate number and type of excipients, as is well known in the art.

[0023] The present nutritional composition or those similarly envisioned by one of skill in the art may be utilized in methods to promote and support a restful period of sleep in an individual.

[0024] Advantageously, the present composition may be used not only as a sole means of promoting and supporting restful sleep but may also be used either in addition to other similarly-directed compositions or as a component of a larger composition. Furthermore, as a component of a greater composition the present invention, may serve to provide a given aspect contributing to the function of broader composition wherein other requirements for good sleep in an individual are addressed by additional compositions.

[0025] Additionally, by way of ingestion of the composition of the present invention, a method for improving the onset of sleep and improvement of sleep quality is provided. The method of the present invention comprises at least the step of administering to an individual a therapeutically acceptable amount of the composition of the present invention.

[0026] Although the following example illustrates the practice of the present invention in one of its example compositional embodiments, the example should not be construed as limiting the scope of the invention. Other embodiments will be apparent to one of skill in the art from consideration of the specifications and example.

Example

[0027] A nutritional supplement to help promote and support restful, quality sleep for use immediately prior to bedtime. A serving of the nutritional supplement as a caplet contains the following:

[0028] About 0.1000 g of an extract of Valerian root standardized to Valerinic acid and about 0.000006 g of Methycobalamin.

Extensions and Alternatives

[0029] In the foregoing specification, the invention has been described with a specific embodiment thereof, however, it will be evident that various modifications

and changes may be made thereto without departing from the broader spirit and scope of the invention.

Claims

What is claimed:

1. A composition comprising an effective amount of an extract of Valerian root and an effective amount Methylcobalamin for promoting sleep in a mammal.

2. The composition of claim 1 wherein the extract of Valerian root agonizes GABA-receptors to induce sedation in a mammal.

3. The composition of claim 1 wherein the extract of Valerian root is standardized to Valerinic Acid.

4. The composition of claim 1 wherein the Methylcobalamin supports the endogenous function of melatonin to maintain normal diurnal rhythms according to a 24-hour cycle.

5. A method of promoting sleep in an individual, the method comprising the step of administering to a mammal a therapeutically effect amount of a composition comprising an extract of Valerian root and Methylcobalamin.

6. The method of claim 5 wherein the extract of Valerian root agonizes GABA-receptors to induce sedation in a mammal.

7. The method of claim 6 wherein the extract of Valerian root is standardized to Valerinic Acid.

8. The method of claim 5 wherein the Methylcobalamin supports the endogenous function of melatonin to maintain normal diurnal rhythms according to a 24-hour cycle.

9. The composition of claim 1, wherein the composition is provided in a layered release solid dosage form.

10. The method of claim 5, wherein the composition is provided in a layered release solid dosage form.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2007/000576

A. CLASSIFICATION OF SUBJECT MATTER

IPC: ***A61K 36/84*** (2006.01) , ***A61K 31/714*** (2006.01) , ***A61K 9/24*** (2006.01) , ***A61P 25/20*** (2006.01) , ***A61P 25/22*** (2006.01)

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 36/84 (2006.01) , ***A61K 31/714*** (2006.01) , ***A61K 9/24*** (2006.01) , ***A61P 25/20*** (2006.01) , ***A61P 25/22*** (2006.01)

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

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)

Scopus, PubMed, Agricola, Delphion, Canadian Patent Database. Keywords: sleep, insomnia, valerian, vitamin B12, valerinic acid, *Valeriana officinalis*, methylcobalamin, Heuer, Clement, Chaudhuri, Thomas, Iomedix, sleep MD

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US20060246129 A1 (LINARDAKIS NM AND WAINWRIGHT NR) 02 November 2006 (02-11-2006) (see abstract, paragraphs 0013, 0026, 0027)	1-10
Y	US6869622 B2 (ANCILE PHARMACEUTICALS INC.) 22 March 2005 (22-03-2005) (see abstract, columns 46-48)	1-10
Y	SHINOMIYA K ET AL. Effects of valerian extract on the sleep wake cycle in sleep disturbed rats. ACTA MEDICA OKAYAMA 2005 59: 89-92 (see whole document)	1-10

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

[X] 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
18 December 2007 (18-12-2007)	8 January 2008 (08-01-2008)

Name and mailing address of the ISA/CA
Canadian Intellectual Property Office
Place du Portage I, C114 - 1st Floor, Box PCT
50 Victoria Street
Gatineau, Quebec K1A 0C9
Facsimile No.: 001-819-953-2476

Authorized officer

Sarita Chaudhary 819- 934-7926

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	OHTA T ET AL. Treatment of persistent sleep-wake schedule disorders in adolescents with methylcobalamin (vitamin B12). SLEEP 1991 14: 414 (see abstract)	1-10
A	BALDERER G AND BORBELY A Effects of valerian on human sleep. PSYCHOPHARMACOLOGY (BERLIN) 1985 87: 406-409	
A	COXETER PD ET AL. Valerian does not appear to reduce symptoms for patients with chronic insomnia in general practice using a series of randomised n-of-1 trials. COMPLEMENTARY THERAPIES IN MEDICINE 2003 11: 215-222	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2007/000576

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [X] Claim Nos. : 5-8 and 10

because they relate to subject matter not required to be searched by this Authority, namely :

Claims 5-8 and 10 are directed to a method for treatment of the human or animal body by surgery or therapy, are not required to be searched by this Authority. Regardless, this Authority has established a search report based on the alleged effect or use of the product defined in these claims.

2. [ ] Claim Nos. :

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

3. [ ] Claim Nos. :

because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2007/000576

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
US20060246129 A1	02-11-2006	None	
US6869622 B2	22-03-2005	AU6366800 A	13-02-2001
		CA2379395 A1	01-02-2001
		EP1235583 A1	04-09-2002
		IL147333D D0	14-08-2002
		JP2003505426T T	12-02-2003
		MXPA02000643 A	21-07-2003
		NZ516531 A	25-10-2002
		US6383526 B1	07-05-2002
		US6913770 B2	05-07-2005
		WO0107063 A1	01-02-2001
		WO02092113 A1	21-11-2002