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(60) **References to other known French documents:**

(71) **Applicant(s):** Pelvipharm SA, France

(72) **Inventor(s):** Giuliano, Francois, and MacKenna, Kevin

(73) **Patentee:**

(74) **Agent:** Cabinet Bardehle Pagenberg and partners.

(54) Medication for the Treatment of Sexual Dysfunction by Acting on the Central Nervous System.

(57) The present invention discloses the use of selegiline and its pharmaceutically acceptable salts in obtaining a medication intended for the treatment of sexual dysfunction in men and women by increasing the libido, arousal, and sexual excitability.

The present invention concerns the treatment of sexual dysfunction in men and women.

The status of recent work on this topic may be found in Erectile Dysfunction (2000) Proceedings of the First International Consultation on Erectile Dysfunction, co-sponsored by W.H.O. and I.C.E.D., Jardin, A.; Wagner, G.; Khoury, S.; Giuliano, F.; Padma-Nathan, H.; Rosen, R. Health Publication Ltd. Oxford 2000.

Very few appropriate treatments are available, especially for women. The preferred mode of administration for the treatment of sexual dysfunction is the oral route, and the active principle should display as few side effects and contraindications as possible.

In this context, most studies have focused on the potential of dopaminergic agonists in the treatment of sexual dysfunction, in men (erectile insufficiency in particular) and in women, including partial or complete absence of desire, absence of orgasm and difficulties with sexual excitability, and these three symptoms may be related.

The action of dopamine on the central nervous system is known both on motivation and on sexual arousal in general, with males as well as females (this knowledge has come mainly from animal experiments) and more precisely on the control of masculine erectile function. In humans, it has been pointed out that certain atypical antidepressants, such as bupropion increase the level of dopamine in the central nervous system and frequently lead to an increase in sexual function, in particular when the person is under the influence of certain psychotropics.

A number of suggestions for the treatment of sexual dysfunction with pharmacological substances that stimulate the central dopaminergic system have been put forward.

A first approach consisted of using a stimulant drug such as amphetamine or cocaine, which increase the production of dopamine and/or inhibit its reuptake. The sexual stimulant effect induced by these drugs has been reported in numerous accounts. However, narcotics are liable to induce drug addiction, which excludes their usage as an unacceptable method to treat sexual dysfunction.

Another more recent approach consists of trying to treat sexual dysfunction with dopamine agonists. US Patent 4521421 thus proposes the use of agonists that are relatively specific to the dopamine D2-receptor for the treatment of sexual dysfunction. US Patents 5985889A and 5945117A suggest the use of a non-specific dopamine receptor agonist, apomorphine, for the treatment of male (erectile insufficiency) and female sexual dysfunction.

However, dopaminergic agonists induce a significant side effect in humans, specifically a marked nausea and vomiting (apomorphine is known for its powerful emetic effect) and also rare cases of fainting.

The aim of the present invention is to propose an active principle useful in the treatment of sexual dysfunction that acts on the central nervous system by stimulation of dopamine without direct stimulation of the dopaminergic receptors.

The invention suggests to that end a new therapeutic indication for selegiline, more specifically the use of selegiline and its pharmaceutically or pharmacologically acceptable salts for a medication intended for the treatment of sexual dysfunction.

Selegiline is an active principle known in its own right. It has a specific inhibitory action on monoamine oxidase B (MAO-B), the enzyme responsible for the degradation of dopamine in the central nervous system. The inhibition of MAO-B involves an increase in the central dopamine levels; moreover, administration of selegiline stimulates the release of dopamine and inhibits its reuptake at the same time, leading to an increased dopaminergic effect.

Selegiline is an active principle that up until the present has been prescribed for the treatment of Parkinson's disease (commercial medicines such as Deprenyl®). The toxicology of the active principle is well known, and it has been demonstrated that it has very few contraindications and undesirable effects. Moreover, selegiline is rapidly absorbed by the oral route (absorption half-life approximately 2.5 hours), a particularly valuable property for the treatment of sexual dysfunction, where it acts rapidly after oral administration.

Selegiline acts on sexual function by several mechanisms. First of all, the increase in dopamine induces a general increase in libido, and it is known that inhibition of libido is a frequent form of sexual dysfunction, particularly in women.

Moreover, the increased dopamine levels in the brain resulting from the administration of selegiline will increase sexual excitement, and it is known that a decrease in the latter is equally important in sexual dysfunction (sexual excitation is necessary to attain orgasm).

Finally, in patients where sexual dysfunction arises from either neurological disorders or peripheral vascular disorders, the administration of selegiline confers the advantage, by increasing excitation, of a stronger neurological stimulation of the genital organs, making it capable of mitigating certain peripheral problems.

The indicated dose is from 5 to 20 mg as needed or as a daily treatment.

Claim

Use of selegiline and its pharmaceutically acceptable salts in obtaining a medication aimed at the treatment of sexual dysfunction in men and women.

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Prior Art Report

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FA 591323
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Documents Considered Pertinent		Affected Claims	INPI classification given to invention
Category	Document Citation with indication of the pertinent part, where necessary		
X	Knoll, J. et al.: "Striatal dopamine, sexual activity and lifespan. Longevity of rats treated with (-) Deprenyl." Life Sciences, GB, Pergamon Press, Oxford, vol. 45, no. 6, 1989, pages 525-531, XP000575063 ISSN: 0024-3205 * page 527, line 6 – page 529, line 8; Figures 1,2 * ---	1	A61K31/135 A61P5/24
X	Dallo, J., et al.: "Age dependent decrease of copulatory activity and its correction by (-) Deprenyl in male rats." Advances in Pharmacological Research and Practice, XX, XX vol. 3, 1985, pages 35-38, XP000575182 * Figure 3 * ---	1	
X	Benet et al.: "The medical treatment of erectile dysfunction." Drugs of Today / Medicamentos de Actualidad, ES, J.R. Prous SS.A. International Publishers, vol. 32, no. 6, September 1, 1996 (1996-09-01), pages 483-499, XP002095494 ISSN: 0025-7656 * page 484, columns 1-2; Table 1 * ---	1	
			Technical Research Domain (Int.CL.7)
X	Morales, A.: "Nonsurgical management options in impotence." Hospital Practice, US, New York, NY, vol.28, no. 3A, March 30, 1993 (1993-03-30), pages 15-16, 19-20, 23-2, XP000645172 * page 20, column 1; Table 2 * ---	1	A61K
X	Dallo, J., et al.: "The ejaculatory behavior of sexually sluggish male rats treated with (-) Deprenyl, apomorphine, bromocriptine and amphetamine." Polish Journal of Pharmacology and Pharmacy, Institute of the Polish Academy of Sciences, PL, vol. 38, no. 3, 1986, pages 251-255, XP000972480 ISSN: 0301-0244 * page 354, paragraph 1; Figure 3 * ---	1	
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Date of Search	Examiner
April 17, 2001	Veronese, A.

Category of Cited Documents

X: especially pertinent by itself
Y: especially pertinent in combination with another document in the same category
A: reflects the state of the art
O: unpublished report
P: published between priority date and application submission date

T: theory or principle fundamental to the invention
E: earlier document, but yet unpublished or having a date after the submission date
D: cited in the patent
L: cited for other reasons

&: member of the same family, corresponding document

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Category	Document Citation with indication of the pertinent part, where necessary		
X	Knoll, J. et al.: "Long-lasting, true aphrodisiac effect of (-) Deprenyl in sexually sluggish old male rats." Modern Problems of Pharmacopsychiatry, CH, Kerger, Basel, vol. 19, 1983, pages 135-153, XP000575123 ISSN: 0077-0094 * entire document *	1	

X	Ferrari, F. et al.: "Inability of (-) Deprenyl to modify copulatory behavior performance in the male rat, whether or not stimulated by the selective D2 dopamine agonist SND 919." Pharmacological Research, GB, Academic Press, London, vol. 29, no. 4, 1994, pages 373-382, XP000866497 ISSN: 1043-6618 * entire document *	1	
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A	US 5 985 889 A (Heaton, Jeremy P. W., et al.) November 16, 1999 (1999-11-16) * entire document *	1	

Date of Search	Examiner
April 17, 2001	Veronese, A.

Category of Cited Documents	
X: especially pertinent by itself Y: especially pertinent in combination with another document in the same category A: reflects the state of the art O: unpublished report P: published between priority date and application submission date	T: theory or principle fundamental to the invention E: earlier document, but yet unpublished or having a date after the submission date D: cited in the patent L: cited for other reasons --- &: member of the same family, corresponding document

Technical Translation by
Matthew F. Schlecht, PhD.
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