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The title of the invention has been amended (Guidelines for Examination in the EPO, A-III, 7.3).

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(54) Use of sertraline for the treatment of premature ejaculation.

(57) A method of treating premature ejaculation comprising administering to a human in need of such treatment an amount of the compound (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine, also known by the generic name sertraline, or a pharmaceutically acceptable salt thereof, effective in delaying ejaculation.

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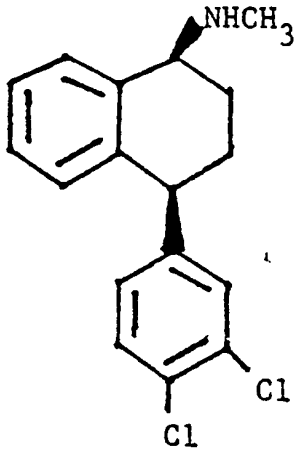
A METHOD OF TREATING PREMATURE EJACULATION USING SERTRALINE

This invention relates to a method of treating premature ejaculation using the compound (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine. hereinafter referred to by its generic name "sertraline", or a pharmaceutically acceptable salt thereof.

Sertraline, which has the empiral formula $C_{12}H_{17}NCl_2$ and the structural formula



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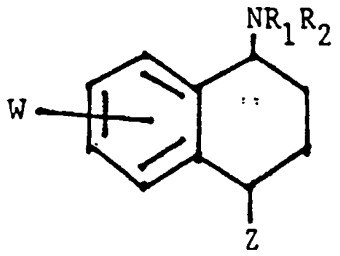
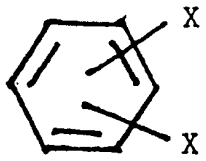
is a known antidepressant and anorectic agent. United States Patent 4,536,518, assigned in common with the present invention and hereby incorporated herein by reference, discloses sertraline and related compounds of the formula



(Cis) I

wherein Z is



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and R_1, R_2, W, X and Y are as defined therein, and states that such compounds exhibit antidepressant and anorectic activity in vivo in mammals.

The present invention relates to a method of treating premature ejaculation, comprising administering to a patient in need of such treatment an amount of sertraline, or a pharmaceutically acceptable salt thereof, effective in delaying ejaculation.

Examples of pharmaceutically acceptable salts of sertraline that can be used to treat premature ejaculation in accordance with the present invention are the acid addition salts of various mineral and organic acids such as hydrochloric, hydrobromic, hydroiodide, sulfuric, phosphoric, acetic, lactic, maleic, fumaric, citric, tartaric, succinic, and gluconic.

Sertraline may be used to delay ejaculation in patients treated with the drug. This effect does not

persist after treatment with the drug is discontinued. Other compounds of the formula I above may be similarly effective.

Sertraline may be prepared as described in United States Patent 4,536,518, and particularly, in Example 2 of that patent.

Sertraline, or a pharmaceutically acceptable salt thereof, when used to treat a premature ejaculation, may be administered either orally or parenterally. It is generally administered in dosages ranging front about 50-200 mg per day, although variations will necessarily occur depending upon the condition of the subject being treated and the particular route of adminisration chosen. It may be administered either alone or in combination with pharmaceutically acceptable carriers by either of the above routes, and such adminisration can be carried out in both single and multiple dosages. More particularly, sertraline, or a pharmaceutically acceptable salt thereof, may be administered in a wide variety of different dosage forms, i.e., it may be combined with various pharmaceutically acceptable inert carriers in the form of tablets, capsules, lozenges, troches, hand candies, powders, sprays, aqueous suspensions, injectable solutions, elixirs, syrups, and the like. Such carriers include solid diluents or fillers, sterile aqueous media and various non-toxic organic solvents, etc. Moreover, such oral pharamaceutical formulations can be suitably sweetened and/or flavored by means of various agents of the type commonly employed for such purposes. In general, sertraline, or a pharmaceutically acceptable salt thereof, when used to treat a chemical dependency, is present in such dosage forms at concentration levels ranging from about 0.5% to about 90% by weight of the total composition, i.e, in amounts that are sufficient to provide the desired unit dosage. It may exist in different polymorphic forms, i.e. different crystalline forms.

For purposes of oral administration, tablets containing various excipients such as sodium citrate, calcium carbonate and calcium phosphate may be employed along with various disintegrants such as starch, preferably potato or tapioca starch, alginic acid and certain complex silicates, together with binding agents such as polyvinylpyrrolidone, sucrose, gelatin and acacia. Additionally, lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc are often very useful for tabletting purposes. Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules; preferred fillers would also include lactose or milk sugar as well as high molecular weight polyethylene glycols. When aqueous suspensions and/or elixers are desired for oral administration, the sertraline, or pharmaceutically acceptable salt thereof, may be combined with various sweetening or flavoring agents, colouring matter or dyes and, if so desired, emulsifying and/or suspending agents, together with diluents such as water, ethanol, propylene glycol, glycerin and various like combinations thereof.

For purposes of parenteral administration, solutions of sertraline, or a pharmaceutically acceptable salt thereof, in sesame or peanut oil or in aqueous propylene glycol or N,N-dimethylformamide may be employed, as well as sterile aqueous solutions of the water-soluble, non-toxic mineral and organic acid addition salts previously enumerated. Such aqueous solutions should be suitably buffered if necessary and the liquid diluent first rendered isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal injection purposes. In this connection, the sterile aqueous media employed are all readily obtainable by standard techniques well-known to those skilled in the art.

A typical dry solid pharmaceutical composition is prepared by blending the following materials together in the proportions by weight specified below:

Cis-(1S)-N-methyl-4-(3,4-dichlorophenyl)-1, 2,3,4-tetrahydro-1-naphthalenamine hydrochloride: 50
Sodium citrate: 25
Alginic acid: 10
Polyvinylpyrrolidone: 10
Magnesium stearate: 5

After the dried composition is thoroughly blended, tablets are punched from the resulting mixture, each tablet being of such size that it contains 100 mg of sertraline hydrochloride. Other tablets are also prepared in a similar fashion containing 5, 10, 25, and 50 mg of sertraline hydrochloride respectively, by using the appropriate amount of the naphthalenamine salt in each case.

Another typical dry solid pharmaceutical composition is prepared by combining the following materials together in the proportions by weight indicated below:

Cis-(1S)-N-methyl-4(3,4-dichlorophenyl)-1,
2,3,4-tetrahydro-1-naphthalenamine hydrochloride: 50
Calcium carbonate: 20
Polyethylene glycol, average molecular weight. 400: 30

The dried solid mixture so prepared is then thoroughly agitated so as to obtain a powdered product that is completely uniform in every respect. Soft elastic and hard-filled gelatin capsules containing this pharmaceu-

tical composition are then prepared, employing a sufficient quantity of material in each instance so as to provide each capsule with 50 mg of the active ingredient.

Claims

1. Use of (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine, or a pharmaceutically acceptable salt thereof, for making a medicament for treatment of premature ejaculation.

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European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number EP 90 30 9063

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Y	"THE MERCK MANUAL OF DIAGNOSIS AND THERAPY", 1987, 15th edition, editor R. Berkow et al., Merck & Co., Inc., Rahway, N.J., US; * Pages 1653,1654,1656,1657 * ---	1	A 61 K 31/135
D,Y	US-A-4 536 518 (W.M. WELCH et al.) * Abstract; claims 1-3,5,7,15,17,19-22 * ---	1	
A	THE JOURNAL OF CLINICAL PSYCHIATRY, vol. 48, no. 3, (suppl.), March 1987, pages 26-30, US; J. MENDELS: "Clinical experience with serotonin reuptake inhibiting antidepressants" * Pages 27,28 * ---	1	
A	US-A-4 507 323 (W.T. STERN) * Abstract; column 1; claim 1 * --- -/-	1	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

A 61 K

INCOMPLETE SEARCH

The Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims

Claims searched completely :

Claims searched incompletely : 1

Claims not searched :

Reason for the limitation of the search:

The subject matter of claim 1 is not supported by pharmacological evidence. In the absence of pharmacological data the evaluation of the technical nature of the subject matter and of the prior art is equivocal and subjective. As a consequence it may well be that relevant prior art has not been retrieved.

Place of search	Date of completion of the search	Examiner
THE HAGUE	13-11-1991	KRAUTBAUER B.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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PARTIAL EUROPEAN SEARCH REPORT

Application Number EP 90 30 9063

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
T	THE JOURNAL OF CLINICAL PSYCHIATRY, vol. 51, no. 12, (suppl. B), December 1990, pages 18-27, US; F.W. REIMHERR et al.: "Antidepressant efficacy of sertraline: A double-blind, placebo- and amitriptyline-controlled, multicenter comparison study in outpatients with major depression" * Abstract; page 24 *	1	
E	EP-A-0 429 189 (PFIZER INC.) * Abstract; page 2; claim 1 *	1	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)

EPO FORM 1503 03.82 (P0401)