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(54) AMELIORATION DE LA MEMOIRE PAR L'ADMINISTRATION DE Δ5-ANDROSTENE-3β-OL-7,17-DIONE ET DE 3β ESTERS DE CELLE-CI

(54) IMPROVING MEMORY BY THE ADMINISTRATION OF Δ5-ANDROSTENE-3β-OL-7,17-DIONE AND 3β ESTERS THEREOF

(57) The memory of a healthy mammal and the memory of a mammal with age impaired memory can be improved by administering an effective amount of Δ5-Androstene-3β-ol-7,17-dione and 3β esters thereof.

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(54) **Title:** IMPROVING MEMORY BY THE ADMINISTRATION OF Δ5–ANDROSTENE–3β–OL–7,17–DIONE AND 3β ESTERS THEREOF

(57) **Abstract**

The memory of a healthy mammal and the memory of a mammal with age impaired memory can be improved by administering an effective amount of Δ5–Androstene–3β–ol–7,17–dione and 3β esters thereof.

IMPROVING MEMORY BY THE ADMINISTRATION OF Δ5-ANDROSTENE-3β-OL-7,17-DIONE AND 3β ESTERS THEREOF

FIELD OF THE INVENTION

The invention relates to the use of pharmaceuticals and dietary supplements to improve memory.

BACKGROUND

Mankind has sought ways to improve memory for years, including efforts ranging from the consumption of specific foods to meditation. While certain of these techniques have demonstrated limited success in improving memory, the search continues for alternative means for improving memory.

SUMMARY OF THE INVENTION

We have discovered that the memory of both a healthy mammal and a mammal with age impaired memory can be improved by administering an effective amount of Δ5-Androstene-3β-ol-7,17-dione and 3β esters thereof.

DETAILED DESCRIPTION OF THE INVENTION INCLUDING A BEST MODE

Definitions

As utilized herein, the term "***healthy mammal***" means a mammal having no diagnosed disease, disorder, infirmity, or ailment known to impair or otherwise diminish memory.

The Steroid

The steroid Δ5-androstene-3β-ol-7,17 dione is a derivative of dehydroepiandrosterone (DHEA) which does not appreciably stimulate, increase or otherwise enhance the production of sex hormones. The steroid is commercially available from a number of sources including Steraloids, Inc. of Newton, Rhode Island. The 3β acetyl form of the steroid is commercially available from Humanetics Corporation of St. Louis Park, Minnesota. A number of procedures are available for synthesizing Δ5-androstene-3β-ol-7,17-dione and the 3β acetyl form from DHEA, with one such procedure described in United States Patent No. 5,296,481.

Precursors of Δ5-androstene-3β-ol-7,17 dione may also be usefully employed for improving memory. Such precursors are readily metabolized *in vivo* to the active Δ5-androstene-3β-ol-7,17 dione. One example of such a metabolizable precursor is the commercially available Δ5-androstene-3β-acetyl-7,17 dione. The 3β-acetyl group is hydrolyzed *in vivo* by esterases located in the blood and various tissues to produce the active Δ5-androstene-3β-ol-7,17 dione, and is believed to be less susceptible to oxidation during the manufacturing process than the hydroxy group found on the active Δ5-androstene-3β-ol-7,17 dione. Other metabolizable precursors include Δ5-androstene-3β, 17β-diol-7-one, Δ5-androstene-3β, 7α-diol-17-one, Δ5-androstene-3β, 7β-diol-17-one and the corresponding esters of these steroids.

Administration

ADMINISTRATION ROUTE

The steroid can be administered by virtually any of the commonly accepted practices for the administration of pharmaceutical preparations including specifically, but not exclusively, mucosal administration, oral consumption, ocular administration, subcutaneous injection, transdermal administration, etc.

Mucosal administration of the steroid includes such routes as buccal, endotracheal, nasal, pharyngeal, rectal, sublingual, vaginal, etc. For administration through the buccal/sublingual/pharyngeal/endotracheal mucosa, the steroid may be formulated as an emulsion, gum, lozenge, spray, tablet or an inclusion complex such as cyclodextrin inclusion complexes. Nasal administration is conveniently conducted through the use of a sniffing power or nasal spray. For rectal and vaginal administration the steroid may be formulated as a cream, douch, enema or suppository.

Oral consumption of the steroid may be effected by incorporating the steroid into a food or drink, or formulating the steroid into a chewable or swallowable tablet.

Ocular administration may be effected by incorporating the steroid into a solution or suspension adapted for ocular application such as drops or sprays.

Subcutaneous administration involves incorporating the steroid into a pharmaceutically acceptable and injectable carrier.

For transdermal administration, the steroid may be conveniently incorporated into a lipophilic carrier and formulated as a topical creme or adhesive patch.

DOSE RATE

The range of dosages and dose rates effective for achieving the desired biological properties and characteristics may be determined in accordance with standard industry practices. These ranges can be expected to differ depending upon whether the desired response is the prophylactic, modulatory, ameliorative or curative in nature.

EXPERIMENTAL

Experiment 1
(Aged Mice)

Aged, two year old mice were tested in the Morris water maze procedure by training the mice to locate the pedestal in less than 15 seconds in three consecutive trials. Immediately upon completion of training one group of mice was treated with DHEA (20 mg/kg) and a second group treated with an eqimolar amount of Δ5-Androstene-3β-acetyl-7,17-dione. Two weeks after treatment the time to rescue was timed in the Morris water maze procedure at: Control 36 seconds, DHEA 27 seconds, and Δ5-Androstene-3β-acetyl-7,17-dione 13 seconds.

Experiment 2
(Scopolamine-Induced Amnesia)

Groups of 13 to 16 C57BL76 mice (35 gm) were tested in the Morris water maze procedure by training the mice to locate the pedestal in less than 15 seconds in three consecutive trials. Immediately upon completion of training the mice in each of three groups were treated with scopolamine (1 mg/kg), scopolamine + DHEA, or scopolamine + Δ5-Androstene-3β-acetyl-7,17-dione. Six days after treatment the average time (sec) to rescue was timed in the Morris water maze procedure at: Control 12.2 ± 1.8; scopolamine 20.0 ± 3.6; scopolamine + DHEA 9.7 ± 1.6; and scopolamine + Δ5-Androstene-3β-acetyl-7,17-dione 8.3 ± 1.8, wherein

control vs. scopolamine p </= 0.055; scopolamine vs. scopolamine + DHEA p </= 0.02; and scopolamine vs. scopolamine + Δ5-Androstene-3β-acetyl-7,17-dione p </= 0.008.

We claim:

1. A method for improving the memory of a healthy mammal comprising the step of administering to the mammal an effective amount of a steroid selected from Δ5-Androstene-3β-ol-7.17-dione and 3β esters thereof.

2. The method of claim 1 wherein the step of administering the steroid to a mammal comprises the step of administering the steroid to a human.

3. The method of claim 2 wherein the method improves the long term memory of the healthy human.

4. The method of claim 2 wherein the step of administering the steroid comprises the step of injecting the steroid.

5. The method of claim 2 wherein the step of administering the steroid comprises the step of inducing ingestion of the steroid.

6. The method of claim 2 wherein the step of administering the steroid comprises the step of administering Δ5-Androstene-3β-acetyl-7,17-dione.

7. A method for improving the memory of a mammal with impaired memory due to aging comprising the step of administering to the mammal an effective amount of a steroid selected from Δ5-Androstene-3β-ol-7,17-dione and 3β esters thereof.

8. The method of claim 7 wherein the step of administering the steroid to a mammal comprises the step of administering the steroid to a human.

9. The method of claim 8 wherein the method improves the long term memory of the human.

10. The method of claim 8 wherein the step of administering the steroid comprises the step of injecting the steroid.

11. The method of claim 8 wherein the step of administering the steroid comprises the step of inducing ingestion of the steroid.

12. The method of claim 8 wherein the step of administering the steroid comprises the step of administering Δ5-Androstene-3β-acetyl-7,17-dione.