THE USE OF OXANDROLONE IN THE TREATMENT OF CHRONIC FATIGUE SYNDROME

The subject invention provides a method of treating chronic fatigue syndrome in a patient suffering from chronic fatigue syndrome which comprises administering an oxandrolone to the patient.
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THE USE OF OXANDROLONE IN THE TREATMENT OF CHRONIC FATIGUE SYNDROME

This application claims priority of U.S. Provisional Application Serial No. 60/032,418, filed December 5, 1996, the contents of which are hereby incorporated into this application by reference. Throughout this specification, various publications are referenced by Arabic numerals within parentheses. Full citations for these references may be found at the end of the specification immediately preceding the claims. The disclosure of these publications in their entireties are hereby incorporated by reference into this specification in order to more fully describe the state of the art to which this invention pertains.

Background of the Invention

Chronic Fatigue Syndrome

Chronic Fatigue Syndrome (CFS) is an illness characterized by fatigue, mild cognitive dysfunction, and in some cases low-grade fever and lymphadenopathy. This illness occurs primarily among adults between the ages of 20 and 40. Although some have speculated that the Epstein Bar Virus (EBV) plays a role in the pathogenesis of CFS, little objective evidence supports this hypothesis (1). CFS may be due to stress and it may also have a psychological component. Chronic fatigue syndrome may have different causes in different people, i.e. different etiology.

There is no approved treatment for chronic fatigue syndrome. Therefore there exists a need for effective treatment of this condition.

CFS is also termed Chronic Fatigue and Immune Dysfunction Syndrome (CFIDS) (7).
Oxandrolone

Oxandrolone (17-methyl-17-hydroxy-2-oxa-5-androstan-3-one) is a known compound which is commercially available. The preparation of oxandrolone is described, inter alia, in U.S. Patent No. 3,128,283. Oxandrolone is an anabolic steroid synthetically derived from testosterone. Oxandrolone has a unique chemical structure compared with other testosterone analogs. Oxandrolone contains an oxygen rather than a carbon atom at the 2-position within the phenanthrene nucleus (2) and lacks a 4-ene function in the A-ring. The anabolic activity of oxandrolone is approximately 6 times greater than its androgenic activity and has been found to be 6.3 times greater than that of methyltestosterone (2).

Anabolic activity refers to the ability to cause nitrogen retention, promoting weight gain and increasing muscle strength. Androgenic activity refers to the ability to enhance male characteristics (i.e. secondary sex characteristics such as facial hais and voice changes). Because of the high ratio of anabolic to androgenic activity, oxandrolone is less likely to cause adverse cosmetic consequences in women than many testosterone analogs.

Furthermore, in contrast to the majority of oral androgenic anabolic steroids (e.g. micronized testosterone, methyltestosterone, fluoxymesterone), oxandrolone undergoes relatively little hepatic metabolism (3, 4).

Oxandrolone has been administered to malnourished patients with alcoholic hepatitis (5, 6). Oxandrolone has been shown to be safe even in dosages of up to 80 mg/day in patients with alcoholic hepatitis (5).

The subject invention discloses the use of an oxandrolone in the treatment of chronic fatigue syndrome.
Summary of the Invention

The subject invention provides a method of treating chronic fatigue syndrome in a patient suffering from chronic fatigue syndrome which comprises administering an oxandrolone to the patient.
Detailed Description of the Invention

Oxandrolone as used herein encompasses 17-methyl-17-hydroxy-2-oxa-5-androstan-3-one (both racemic mixtures and optically active enantiomers) as well as pharmaceutically acceptable esters thereof. For example, an oxandrolone product which is commercially available is the Oxandrin® tablet from BTG Pharmaceuticals Corp., Iselin, NJ 08830, which is 17α-methyl-17β-hydroxy-2-oxa-5α-androstan-3-one. This product was used throughout the studies described herein.

Oxandrolone may be administered orally, intravenously, intramuscularly, subcutaneously, topically, intratracheally, intrathecally, intraperitoneally, rectally, vaginally or intrapleurally.

If oxandrolone is administered orally, it is administered in the form of a tablet, a pill, a liquid or a capsule.

A liquid may be administered in the form of a solution or a suspension.

The compositions produced in accordance with the invention may comprise conventional pharmaceutically acceptable diluents or carriers. Tablets, pills, liquids and capsules may include conventional excipients such as lactose, starch, cellulose derivatives, hydroxypropyl methylcellulose and magnesium stearate. Suppositories may include excipients such as waxes and glycerol. Injectable solutions will comprise sterile pyrogen-free media such as saline and may include buffering agents, stabilizing agents, solubilizing agents or preservatives. Conventional enteric coatings may also be used.

Compositions for topical administration may be in the form of creams, ointments, lotions, solutions, transdermal delivery systems, transdermal patches or gels.
Oxandrolone may be administered in a solid dosage form, in a liquid dosage form, in a sustained-release formulation or in a once a day formulation. The liquid dosage form may _inter alia_ be alcohol-based or formulated with a cyclodextrin such as hydroxypropyl-β-cyclodextrin.

The subject invention provides a method of treating chronic fatigue syndrome in a patient suffering from chronic fatigue syndrome which comprises administering a therapeutically effective amount of an oxandrolone to the patient.

The subject invention also provides a method of treating a symptom associated with chronic fatigue syndrome in a patient suffering from chronic fatigue syndrome which comprises administering a therapeutically effective amount of an oxandrolone to the patient.

In a preferred embodiment, the amount of the oxandrolone is about 1-100 mg per day.

In an especially preferred embodiment, the amount of the oxandrolone is about 5-20 mg per day.

The subject invention further provides a use of an oxandrolone in the preparation of a composition to treat chronic fatigue syndrome.

Interferon as used herein encompasses any interferon such as alpha-interferon, beta-interferon or gamma-interferon.

Corticosteroid as used herein encompasses _inter alia_ glucocorticoids, mineralcorticoids and androgens. Examples of glucocorticoids are hydrocortisone, cortisone, corticosterone and synthetic analogs of hydrocortisone and cortisone (such as cortisol, prednisolone and prednisone). Examples of mineralcorticoids are aldosterone and desoxycorticosterone. Examples of androgens are DHEA, androstenedione, testosterone and 11β-
hydroxyandrostenedione.

The oxandrolone may be administered in conjunction with a corticosteroid, an interferon or any known anti-inflammatory agent.

Oxandrolone may also be administered in conjunction with glutamine or human growth hormone.

Oxandrolone may also be administered in conjunction with nutritional counselling and exercise.
Examples

The Examples which follow are set forth to aid in understanding the invention but are not intended to, and should not be construed to, limit its scope in any way.

EXAMPLE 1: The Effect of Oxandrolone in the Treatment of Patients Suffering from Chronic Fatigue Syndrome

Several patients are being treated with Oxandrin*, with preliminary good results:

Women are treated with 2.5mg twice a day and men with 5mg twice a day, and the dosage is increased as necessary, up to 20mg per day (i.e. 10mg twice a day).

Oxandrolone caused an improvement in the condition of CFS patients. The criteria for measuring this improvement are based on subjective reporting from the patients who felt better, had more energy, could do more and spend less time in bed during the daytime.

A quality of life questionnaire showed improved quality of life in these patients which also demonstrates the efficacy of oxandrolone as a treatment in CFS patients.
EXAMPLE 2: Seven Case Histories:

1) L. - 52 year old white female with four children. L. has a 10 year history of CFIDS with severe fatigue, cognitive dysfunction, and tachycardia. She also has a high cholesterol level.

Protocol: 0.6 grams/lb protein (20% of total calories)
protein supplement
15 minutes progressive resistance exercise (PRE) 4x/wk (4 times per week)
Oxandrin 5 mg bid

Results after 10 months- patient improving

2) M. - 30 year old white male, no children. He has an 8 year history of CFI.

Protocol: 0.6 grams/lb protein (20% of total calories)
20 minutes PRE’s every other day
Oxandrin 10 mg bid

Results after 11 months- patient improving

3) E. - 55 year old divorced white female, two grown children. She has a 10 year history of CFIDS with severe fatigue, dizziness and cognitive dysfunction.

Protocol: 0.6 grams/lb protein (20% of total calories)
15 minutes PRE’s every other day
Oxandrin 2.5 mg bid

Results after 9 months- patient improving

4) W. - 35 year old single white male. W. has 4 year history of CFIDS with severe fatigue, diarrhea and frequent flu-like episodes.
Protocol: 0.6 grams/lb protein (20% of total calories)
20 minutes PRE's every other day
Oxandrin 10 mg bid

Results after 9 months- patient improving

5) J.P. - 35 year old white female. J.P. has a 4 year history of CFIDS with severe fatigue, diarrhea and frequent flu-like episodes.

Protocol: 0.6 grams/lb protein (20% of total calories)
20 minutes PRE's 4x/wk
Oxandrin 10 mg bid

Result- patient intolerant

6) J.E. - 35 year old single white female. J.E. has a 14 year old history of CFIDS with severe fatigue dating back to acute viral illness in 1983, anxiety, depression, chronic HA's, intermittent ulcerative proctitis, mitral valve prolapse and other symptoms.

Protocol: 80 grams protein/day (60% of body weight)
15 minutes PRE's 4x/wk
Oxandrin 5 mg bid

Results after 9 months- patient improving

7) R.R. - 45 year old white male. R.R. has a 17 year history of chronic fatigue and mild depression. His energy level was improved by antidepressants but he was unable to tolerate them for any extended period of time secondary to insomnia. R.R. was also unable to tolerate Oxandrin® secondary to insomnia.

Result- patient intolerant

Five out of seven patients experienced significant
improvement with oxandrolone treatment.
References


What is claimed is:

1. A method of treating chronic fatigue syndrome in a patient suffering from chronic fatigue syndrome which comprises administering a therapeutically effective amount of an oxandrolone to the patient.

2. A method of treating a symptom associated with chronic fatigue syndrome in a patient suffering from chronic fatigue syndrome which comprises administering a therapeutically effective amount of an oxandrolone to the patient.

3. A method according to claims 1 or 2 wherein the amount of the oxandrolone is about 1-100 mg per day.

4. A method according to claim 3 wherein the amount of the oxandrolone is about 5-20 mg per day.

5. A method according to claims 1 or 2, wherein the oxandrolone is 17α-methyl-17β-hydroxy-2-oxa-5α-androstan-3-one.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) : A61K 31/585
US CL : 514/175
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)
U.S. : 514/175
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
APS AND CAS ONLINE: oxandrolone with cfs, chronic fatigue, tired, fatigue

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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Date of the actual completion of the international search
27 JANUARY 1998

Date of mailing of the international search report
27 FEB 1998

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