development of AIMs. Based on these observations, it has been accepted that rats lesioned with 6-OHDA exhibit motor deficits that share essential functional similarities with Parkinson's dyskinesia and can be used to evaluate the potential of a treatment to provide treatments for dyskinesia.

In an attempt to identify new therapies for treating dyskinesia and other related movement disorders, applicants have surprisingly found that (4aR,10aR)-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol as a potent D1/D2 agonist [herein referred to as Compound **10**]; (6aR,10aR)-7-*n*-propyl-6,6a,7,8,9,10,10a,11-octahydro-1,3-dioxa-7-aza-cyclopenta[a]anthracene [herein referred to as Compound **11**]; and (4aR,10aR)-1-*n*-propyl-2,3,4,4a,5,7,8,9,10,10a-decahydro-1H-benzo[g]quinolin-6-one [herein referred to as Compound **12**] have favorable profiles in rats with unilateral 6-OHDA lesions. They induce less dyskinesias than L-DOPA and apomorphine, and reduce L-DOPA induced dyskinesias more effectively than D2 agonists, as exemplified by pramipexole. Hence, Compounds **10, 11 and 12** have the potential to become the first PD drugs with L-DOPA-like efficacy and a favorable profile not only in terms of both induction of dyskinesia, but also as a medication for the reversal of dyskinesias.

Accordingly, it is expected that above identified compounds can be used to treat dyskinesias and other related movement disorders such as Huntington's chorea. Moreover, the present invention contemplates the use of the corresponding racemic *trans* mixture. The present invention further provides methods of treating Parkinson's disease with a low dyskinesia induction profile comprising administering a therapeutically effective amount of said compound. In one aspect, the treatment of Parkinson's disease is as efficacious as L-DOPA treatment. Further provided are methods of reversing dyskinesias or treating Parkinson's disease comprising administering said compound and pharmaceutical compositions thereof.

SUMMARY OF THE INVENTION

In o~~O~~ne aspect, there is provided ~~of the invention is concerned with~~ the use of (4aR,10aR)-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

Another ~~aspect~~embodiment relates to the use of racemic *trans*-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol in the preparation of a medicament for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

A separate ~~aspect~~embodiment of the ~~invention~~disclosure relates to the use of (4aR,10aR)-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol or a pharmaceutically acceptable salt thereof, in the preparation of a medicament treating Parkinson's disease.

Another ~~aspect~~embodiment relates to the use of racemic *trans*-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol in the preparation of a medicament for treating Parkinson's disease.

In a~~A~~ separate aspect, there is provided ~~of the invention relates to~~ the use of (4aR,10aR)-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for reversing dyskinesias.

Another ~~aspect~~embodiment relates to the use of racemic *trans*-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol in the preparation of a medicament for reversing dyskinesias.

Another ~~aspect~~embodiment is directed to a pharmaceutical composition comprising (4aR,10aR)-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol or a pharmaceutically acceptable salt thereof, for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

Separate ~~aspects~~embodiments of the ~~invention~~disclosure relate to a pharmaceutical composition comprising racemic *trans*-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol in the preparation of a medicament for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

Another ~~aspect~~embodiment is directed to a method of treating Parkinson's disease while maintaining a low dyskinesia induction profile comprising administering a therapeutically effective amount of (4aR,10aR)-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol or a pharmaceutically acceptable salt thereof.

A separate ~~aspect~~embodiment relates to a method of treating Parkinson's disease while maintaining a low dyskinesia induction profile a low dyskinesia induction profile comprising administering a

therapeutically effective amount of racemic *trans*-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol .

Another ~~aspect~~embodiment is directed to a method of reversing dyskinesias comprising administering a therapeutically effective amount of (4aR,10aR)-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol or a pharmaceutically acceptable salt thereof.

Yet another ~~aspect~~embodiment is directed to a method of reversing dyskinesias comprising administering a therapeutically effective amount of racemic *trans*-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol or a pharmaceutically acceptable salt thereof.

In o~~O~~ne aspect, there is provided ~~of the invention is concerned with~~ the use of (6aR,10aR)-7-*n*-propyl-6,6a,7,8,9,10,10a,11-octahydro-1,3-dioxa-7-aza-cyclopenta[a]anthracene or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

In a~~A~~ separate aspect, there is provided ~~of the invention relates to~~ the use of (6aR,10aR)-7-*n*-propyl-6,6a,7,8,9,10,10a,11-octahydro-1,3-dioxa-7-aza-cyclopenta[a]anthracene or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for reversing dyskinesias.

Another ~~aspect~~embodiment is directed to a pharmaceutical composition comprising (6aR,10aR)-7-*n*-propyl-6,6a,7,8,9,10,10a,11-octahydro-1,3-dioxa-7-aza-cyclopenta[a]anthracene or a pharmaceutically acceptable salt thereof, for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

Separate ~~aspects~~embodiments of the ~~invention~~disclosure relate to a pharmaceutical composition comprising (6aR,10aR)-7-*n*-propyl-6,6a,7,8,9,10,10a,11-octahydro-1,3-dioxa-7-aza-cyclopenta[a] anthracene or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

Another ~~aspect~~embodiment is directed to a method of treating Parkinson's disease while maintaining a low dyskinesia induction profile comprising administering a therapeutically effective amount of (6aR,10aR)-7-*n*-propyl-6,6a,7,8,9,10,10a,11-octahydro-1,3-dioxa-7-aza-cyclopenta[a] anthracene or a pharmaceutically acceptable salt thereof.

Another ~~aspect~~embodiment is directed to a method of reversing dyskinesias comprising administering a therapeutically effective amount of (6aR,10aR)-7-*n*-propyl-6,6a,7,8,9,10,10a,11-octahydro-1,3-dioxa-7-aza-cyclopenta[a]anthracene or a pharmaceutically acceptable salt thereof.

One ~~aspect~~embodiment of the ~~invention~~disclosure is concerned with the use of (4aR,10aR)-1-*n*-propyl-2,3,4,4a,5,7,8,9,10,10a-decahydro-1H-benzo[g]quinolin-6-one, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating Parkinson's disease while maintaining a low dyskinesia induction profile

A separate ~~aspect~~embodiment of the ~~invention~~disclosure relates to the use of (4aR,10aR)-1-*n*-propyl-2,3,4,4a,5,7,8,9,10,10a-decahydro-1H-benzo[g]quinolin-6-one, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating Parkinson's disease.

In y~~Y~~et another aspect, there is provided ~~relates to~~ the use of (4aR,10aR)-1-*n*-propyl-2,3,4,4a,5,7,8,9,10,10a-decahydro-1H-benzo[g]quinolin-6-one, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for reversing dyskinesias.

Another ~~aspect~~embodiment is directed to a pharmaceutical composition comprising (4aR,10aR)-1-*n*-propyl-2,3,4,4a,5,7,8,9,10,10a-decahydro-1H-benzo[g]quinolin-6-one, or a pharmaceutically acceptable salt thereof, for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

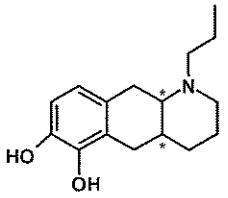
Separate ~~aspects~~embodiments of the ~~invention~~disclosure relate to a pharmaceutical composition comprising (4aR,10aR)-1-*n*-propyl-2,3,4,4a,5,7,8,9,10,10a-decahydro-1H-benzo[g]quinolin-6-one or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for treating Parkinson's disease while maintaining a low dyskinesia induction profile.

Another ~~aspect~~embodiment is directed to a method of treating Parkinson's disease while maintaining a low dyskinesia induction profile comprising administering a therapeutically effective amount of (4aR,10aR)-1-*n*-propyl-2,3,4,4a,5,7,8,9,10,10a-decahydro-1H-benzo[g]quinolin-6-one or a pharmaceutically acceptable salt thereof.

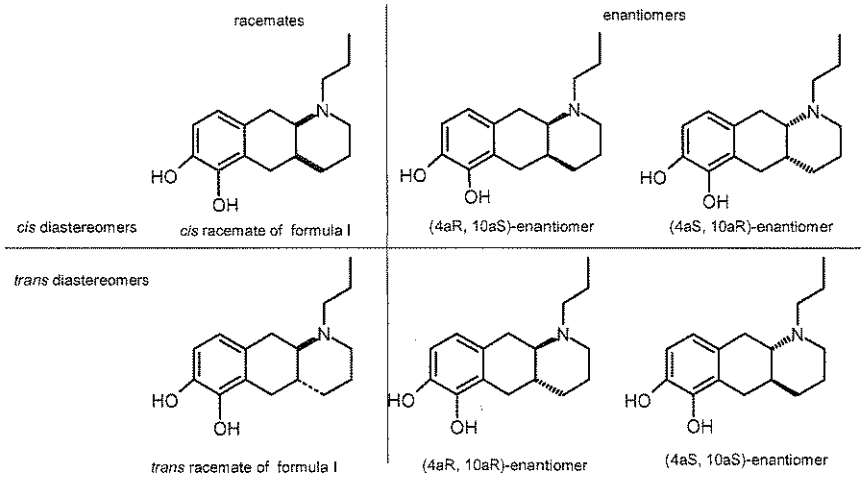
Another ~~aspect~~embodiment is directed to a method of reversing dyskinesias comprising administering a therapeutically effective amount of (4aR,10aR)-1-*n*-propyl-2,3,4,4a,5,7,8,9,10,10a-decahydro-1H-benzo[g]quinolin-6-one or a pharmaceutically acceptable salt thereof.

DETAILED DESCRIPTION

The compounds of the present invention contain two chiral centers (denoted with * in the below formula)



The compounds of the invention can exist in two different diastereomeric forms, the *cis*- and *trans*-isomers, both of which can exist in two enantiomeric forms. The present invention relates only to the *trans* racemate and the (4aR, 10aR)-enantiomer.



As previously indicated, the present invention is based on the discovery that (4aR,10aR)-1-*n*-propyl-1,2,3,4,4a,5,10,10a-octahydro-benzo[g]quinoline-6,7-diol (herein referred to as "Compound **10**") reversed dyskinesias induced by L-DOPA/benserazide and apomorphine in rats lesioned with 6-OHDA. The corresponding *trans* racemate also falls within the scope of this invention.

Additionally, the compound of the present invention contain two chiral centers (denoted with * in the below formula)