mexiletine, sulfisoxazole and torasemide, or a salt, prodrug, derivative of any chemical purity, or sustained-release formulation thereof.

Preferred examples of drug combinations include, *e.g.*, baclofen and acamprosate, baclofen and cinacalcet, mexiletine and cinacalcet, torasemide and baclofen, or torasemide and sulfisoxazole. In a particular embodiment, the compositions and methods further comprise Levodopa.

The compositions may further comprise one or several pharmaceutically acceptable carrier(s) or excipient(s), and they may be administered repeatedly to the subject. Preferred compositions are administered orally. Moreover, the drugs may be formulated or administered together, separately or sequentially.

The disclosed compositions are suitable for treating Parkinsonism in any mammalian subject, particularly in a human subject, at any stage of the disease. The disclosure may be used *e.g.*, to retard the development of the disease, to reduce, delay or prevent tremor, hypokinesia (*e.g.*, bradykinesia, akinesia, rigidity) postural instability, and/or pain, and/or to increase survival.

One aspect of the disclosure~~invention~~ relates to the use of a composition comprising acamprosate and baclofen or ~~a~~ salt(s), ~~prodrug, derivative of any chemical purity,~~ or sustained release formulation(s) thereof, in the manufacture of a medicament for the treatment of Parkinson's disease~~parkinsonism~~.

In another aspect, there is provided a composition comprising baclofen, acamprosate and levodopa or any pharmaceutically acceptable salts thereof.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1: Effect of cinacalcet and mexiletine combination therapy against glutamate toxicity on neuronal cortical cells. The glutamate intoxication is significantly prevented by the combination of cinacalcet (64 pM) and mexiletine (25.6 pM) whereas, at those concentrations, cinacalcet and mexiletine alone have no significant effect on intoxication. *: $p<0.001$, significantly different from glutamate intoxication; (ANOVA + Dunnett Post-Hoc test).

Figure 2: Effect of sulfisoxazole and torasemide combination therapy against glutamate toxicity on neuronal cortical cells. The glutamate intoxication is significantly prevented by the combination of sulfisoxazole (6.8 nM) and torasemide (400 nM) whereas, at those concentrations, sulfisoxazole and torasemide alone have no significant effect on intoxication.*: $p<0.001$, significantly different from glutamate intoxication; (ANOVA + Dunnett Post-Hoc test).

CLAIMS

1. Use of a composition comprising acamprosate and baclofen or ~~a~~ salt(s), ~~prodrug, derivative of any chemical purity,~~ or sustained release formulation(s) thereof, in the manufacture of a medicament for use in the treatment of ~~parkinsonism~~ Parkinson's disease in a subject in need thereof.

~~2. The use of claim 1, wherein parkinsonism is a condition selected from Parkinson's disease, progressive supranuclear palsy, multiple system atrophy, cortical basal ganglionic degeneration, diffuse Lewy body disease, Parkinson's dementia, X linked dystonia parkinsonism, and secondary parkinsonism.~~

~~3. The use of claim 1, wherein said medicament is for treating Parkinson's disease.~~

4.2. The use of claim 1 ~~or 3~~, wherein said medicament comprises at least one of the following drug combinations:
   - baclofen and acamprosate and cinacalcet,
   - baclofen and acamprosate and torasemide, or
   - baclofen and acamprosate and mexiletine.

5.3. The use of any one of claims 1 ~~4~~ or 2, the medicament further comprising at least one dopamine precursor, at least one dopamine

receptor agonist, and/or at least one inhibitor of dopamine metabolizing enzymes.

6.4. The use of claim 53, wherein the at least one dopamine precursor is selected from the group consisting of levodopa and melevodopa, or salts, ~~prodrugs, derivative of any purity~~ or sustained release formulations thereof the at least one dopamine receptor agonist is selected from the group consisting of talipexole, piribedil, rotigotine, bromocriptine, pergolide, cabergoline, lisuride, pramipexole, ropinirole or apomorphine, or salts~~, prodrugs, derivative of any purity~~ or sustained release formulations thereof and the at least one inhibitor of dopamine metabolizing enzymes is selected from the group consisting of selegiline and rasagiline, or salts~~, prodrugs, derivative of any purity~~ or sustained release formulations thereof.

7.5. The use of claim 53 or 64, the medicament comprising at least one of the following drug combinations:

- baclofen and acamprosate and levodopa,
- baclofen and acamprosate and cinacalcet and levodopa,
- baclofen and acamprosate and torasemide and levodopa, or
- baclofen and acamprosate and mexiletine and levodopa.

8.6. The use of claim 75, the medicament further comprising carbidopa or a salt~~, prodrug, derivative of any purity~~ or sustained release formulation thereof.

9.7. The use of any one of the preceding claims, the medicament further comprising a pharmaceutically acceptable carrier or excipient.

10.8. The use of any one of the preceding claims, wherein the compounds are formulated or administered together, separately or sequentially.

~~11.~~9. The use of any one of the preceding claims, wherein said medicament is to be administered repeatedly to the subject.

~~12.~~10. The use of any one of the preceding claims, wherein said medicament is to be administered orally.

~~13.~~11. The use of any one of claims 1 to ~~11~~10, wherein acamprosate is provided in said medicament in a dosage of less than 50 mg per day, or less than 10 mg per day.

~~14.~~12. The use of any one of claims 1 to ~~12~~11, wherein baclofen is provided in said medicament in a dosage of less than 30 mg per day.

~~15.~~13. The use of any one of claims 1 to ~~14~~12, for protecting dopaminergic neurons of the nigrostriatal system from degeneration.

~~16.~~14. The use of any one of claims 1 to ~~14~~12, for the treatment of bradykinesia or akinesia.

~~17.~~15. The use of any one of the preceding claims ~~1~~, wherein said subject in need thereof is also treated with deep brain stimulation of the subthalamic nucleus or of the globus pallidus interna.

~~18.~~16. The use of any one of the preceding claims, for preventive treatment in a subject in need thereof and at risk of parkinsonism.

~~19.~~17. A composition comprising baclofen, acamprosate and levodopa or any pharmaceutically acceptable salts thereof.

18. The composition of claim 17, further comprising carbidopa, or a salt or sustained release formulation thereof.