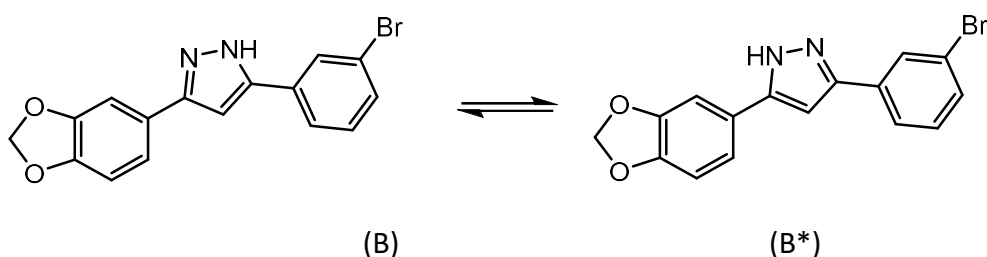


the fatty acid is independently selected from C₈-C₂₂ fatty acids; and

the polyethylene glycol is independently selected from polyethylene glycols containing about 20 to about 40 ethylene oxide units. In some examples, the PEG contains about 32 ethylene oxide units. In some examples, the fatty acid is independently selected from C₈-C₁₈ fatty acids.

In particular examples, the pharmaceutical composition comprises a compound wherein each of R, R^{E7} and R^{E8} is H and Hal is Br, the compound having the general formula (B), (B*)



or a mixture thereof.

The excipient can further comprise a monoglyceride of a fatty acid, a diglyceride of a fatty acid and/or a triglyceride of a fatty acid, wherein the fatty acid is independently selected from C₈-C₂₂ fatty acids. The excipient can further comprise a polyethylene glycol (PEG) containing about 20 to about 40 ethylene oxide units, and in specific examples, about 32 ethylene oxide units. In some examples, the fatty acid is independently selected from C₈-C₁₈ fatty acids.

In some examples, the excipient comprises a mixture of monoesters of fatty acids and polyethylene glycol and/or diesters of fatty acids and polyethylene glycol, wherein the fatty acids maybe derived from a natural source, for example a plant source including coconut oil and/or hydrogenated coconut oil. In particular examples, the excipient comprises a mixture of monoesters of fatty acids and polyethylene glycol and/or diesters of fatty acids and polyethylene glycol, wherein the fatty acids comprise up to 15 wt% caprylic acid (C8), up to 12 wt% capric acid (C10), 30 to 50 wt% lauric acid (C12), 5 to 25 wt% myristic acid (C14), 4 to 25 wt% palmitic acid (C16), and 5 to 35 wt% stearic acid (C18).

In some examples, the excipient comprises about 50 wt% to about 80 wt%, preferably about 60 wt% to about 75 wt%, more preferably about 72 wt%, of the at least one

monoester of a fatty acid and polyethylene glycol and/or the at least one diester of a fatty acid and polyethylene glycol. In some examples, the excipient further comprises about 10 wt% to about 30 wt%, preferably about 15 wt% to about 25 wt%, more preferably about 20 wt%, of the monoglyceride of the fatty acid, the diglyceride of the fatty acid and/or the triglyceride of the fatty acid. In some examples, the excipient further comprises about 5 wt% to about 20 wt%, preferably about 5 wt% to about 10 wt%, more preferably about 8 wt%, of the polyethylene glycol containing about 20 to about 40 ethylene oxide units, or about 32 ethylene oxide units.

The excipient can have a melting range in the range of about 33 °C to about 64 °C, preferably about 35 °C to about 55 °C, more preferably about 42.5 °C to about 47.5 °C, even more preferably about 44 °C. In some examples, the excipient has a hydrophilic lipophilic balance (HLB) of about 1 to about 16, preferably from about 7 to about 14, about 11 or about 14.

The process of obtaining the excipient is not limited. The excipient may be obtained by for example, an alcoholysis reaction between the polyethylene glycol and a triglyceride of the fatty acid or by polyglycolysis of hydrogenated vegetable oil with PEG, for example hydrogenated coconut oil or palm kernel oil with a PEG, for example PEG-32.

In some examples, the pharmaceutical composition comprises about 3 wt% to about 5 wt% of the compound having the general formula (A) or (A*) or a mixture thereof and about 95 wt% to about 97 wt% of the excipient, based on 100 wt% of the total pharmaceutical composition. In particular examples, the pharmaceutical composition comprises about 3 wt% to about 5 wt% of the compound having the general formula (B) or (B*) or a mixture thereof and about 95 wt% to about 97 wt% of the excipient, based on 100 wt% of the total pharmaceutical composition.

Further provided is an oral dosage form comprising the pharmaceutical described herein. The oral dosage form may be in the form of a capsule, for example a HPMC capsule or a gelatin capsule. In some examples the oral dosage form comprises from about 1 mg to about 100 mg of the compound, i.e. a compound of formulae (A), (A*), or mixtures thereof or (B), (B*), or mixtures thereof, from about 5 mg to about 50 mg of the compound, or from about 10 mg to about 30 mg of the compound. In another aspect, provided herein is an

oral dosage form comprising the pharmaceutical composition as described herein, the dosage form comprising about 1mg to about 100 mg of the compound, or about 5 mg to about 50 mg of the compound, preferably about 10 mg or about 30 mg of the compound.

Further provided herein are methods of treating or preventing a disease linked to protein aggregation and/or a neurodegenerative disease, for example an α -synucleinopathy, wherein a therapeutically effective amount of the pharmaceutical composition or oral dosage form disclosed herein is administered to a patient in need thereof. Further provided is the pharmaceutical composition or the oral dosage form for use in the treatment or prevention of a disease linked to protein aggregation and/or a neurodegenerative disease, for example, in the treatment or prevention of an α -synucleinopathy. In another aspect, provided herein is the pharmaceutical composition as described herein or the oral dosage form as described herein, for use in therapy. In addition, provided is a compound selected from formulae (A), (A*), or mixtures thereof or (B), (B*), or mixtures thereof, and a pharmaceutically acceptable excipient comprising at least one monoester of a fatty acid and polyethylene glycol and/or at least one diester of a fatty acid and polyethylene glycol,

wherein the fatty acid is independently selected from C₈-C₂₂ fatty acids; and

the polyethylene glycol is independently selected from polyethylene glycols containing about 20 to about 40 ethylene oxide units,

for the manufacture of a medicament for the treatment or prevention of a disease linked to protein aggregation and/or a neurodegenerative disease, for example, in the treatment or prevention of an α -synucleinopathy. In another aspect, provided herein is use of the pharmaceutical composition as described herein or the oral dosage form as described herein, in the manufacture of a medicament for the treatment or prevention of a disease linked to protein aggregation and/or a neurodegenerative disease. The α -synucleinopathy can be selected from multiple system atrophy (MSA), Parkinson's disease (PD), or dementia with Lewy bodies (DLB), preferably multiple system atrophy (MSA). The pharmaceutical composition or medicament may be administered orally and is to be administered to a subject without regard to food intake.

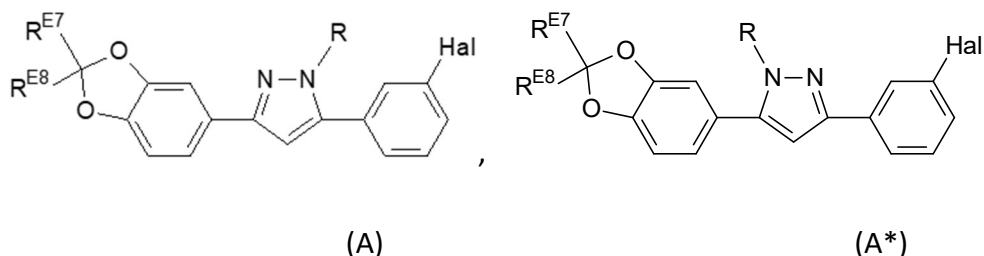
Further provided are pharmaceutical compositions, unit dosage forms, and methods, according to any of the following clauses:

1. A pharmaceutical composition comprising a compound of formula (A), (A*) or a mixture thereof and an excipient comprising lauroyl polyoxyl-32 glycerides, the lauroyl polyoxyl-32 glycerides comprising a mixture of mono-, di- and triglycerides, PEG fatty acid monoesters and/or diesters, and free PEG.
2. The pharmaceutical composition of clause 1, comprising a compound of formula (B), (B*) or a mixture thereof and an excipient comprising lauroyl polyoxyl-32 glycerides, the lauroyl polyoxyl-32 glycerides comprising a mixture of mono-, di- and triglycerides, PEG fatty acid monoesters and/or diesters, and free PEG.

CLAIMS

1. A pharmaceutical composition comprising:

at least one compound having the general formula (A) or (A*)



or a stereoisomer, racemate, hydrate or solvate thereof,

wherein

R is selected from hydrogen; C₁₋₄ alkyl; and -C₁₋₄ alkylene-halogen;

Hal is selected from F, Cl, Br, and I; and

R^{E7} and R^{E8} are independently H or F;

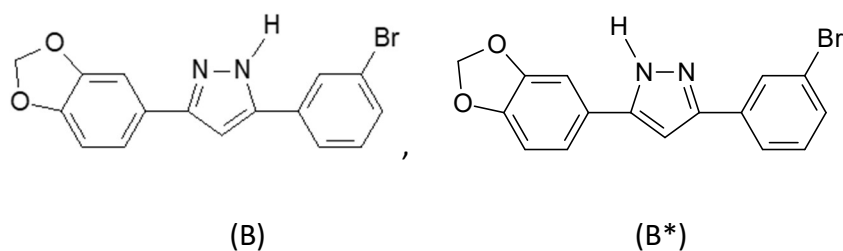
and a pharmaceutically acceptable excipient, wherein the excipient comprises at least one monoester of a fatty acid and polyethylene glycol and/or at least one diester of a fatty acid and polyethylene glycol,

wherein

the fatty acid is independently selected from C₈-C₂₂ fatty acids; and

the polyethylene glycol is independently selected from polyethylene glycols containing about 20 to about 40 ethylene oxide units.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises a compound having the general formula (B), (B*)



or a mixture thereof.

3. The pharmaceutical composition of claim 1 or 2, wherein the excipient further comprises a monoglyceride of a fatty acid, a diglyceride of a fatty acid and/or a triglyceride of a fatty acid, wherein the fatty acid is independently selected from C₈-C₂₂ fatty acids, preferably C₈-C₁₈ fatty acids.
4. The pharmaceutical composition of any one of claims 1 to 3, wherein the polyethylene glycol contains about 32 ethylene oxide units.
5. The pharmaceutical composition of any one of claims 1 to 4, wherein the excipient further comprises a polyethylene glycol containing about 20 to about 40 ethylene oxide units, preferably about 32 ethylene oxide units.
6. The pharmaceutical composition of any one of claims 1 to 5, wherein the fatty acid comprises lauric acid, preferably wherein the fatty acid comprises 30 to 50 wt% lauric acid based on the total weight of fatty acids.
7. The pharmaceutical composition of any one of claims 1 to 6, wherein the excipient comprises a mixture of monoesters of fatty acids and polyethylene glycol and/or diesters of fatty acids and polyethylene glycol, wherein the fatty acids are derived from coconut oil and/or hydrogenated coconut oil.
8. The pharmaceutical composition of any one of claims 1 to 7, wherein the excipient comprises a mixture of monoesters of fatty acids and polyethylene glycol and/or diesters of fatty acids and polyethylene glycol, wherein the fatty acids comprise
up to 15 wt% caprylic acid (C₈),
up to 12 wt% capric acid (C₁₀),
30 to 50 wt% lauric acid (C₁₂),
5 to 25 wt% myristic acid (C₁₄),
4 to 25 wt% palmitic acid (C₁₆), and
5 to 35 wt% stearic acid (C₁₈).

9. The pharmaceutical composition of any one of claims 1 to 8, wherein the excipient comprises about 50 wt% to about 80 wt%, preferably about 60 wt% to about 75 wt%, more preferably about 72 wt%, of the at least one monoester of a fatty acid and polyethylene glycol and/or the at least one diester of a fatty acid and polyethylene glycol.
- 5 10. The pharmaceutical composition of any one of claims 3 to 9, wherein the excipient comprises about 10 wt% to about 30 wt%, preferably about 15 wt% to about 25 wt%, more preferably about 20 wt%, of the monoglyceride of the fatty acid, the diglyceride of the fatty acid and/or the triglyceride of the fatty acid.
- 10 11. The pharmaceutical composition of any one of claims 5 to 10, wherein the excipient comprises about 5 wt% to about 20 wt%, preferably about 5 wt% to about 10 wt%, more preferably about 8 wt%, of the polyethylene glycol containing about 20 to about 40 ethylene oxide units.
- 15 12. The pharmaceutical composition of any one of claims 1 to 11, wherein the excipient is obtained by an alcoholysis reaction between the polyethylene glycol and a triglyceride of the fatty acid.
13. The pharmaceutical composition of any one of claims 1 to 12, wherein the excipient has a melting range in the range of about 33 °C to about 64 °C, preferably about 35 °C to about 55 °C, more preferably about 42.5 °C to about 47.5 °C, even more preferably about 44 °C.
- 20 14. The pharmaceutical composition of any one of claims 1 to 13, wherein the excipient has a hydrophilic lipophilic balance (HLB) of about 1 to about 16, preferably from about 7 to about 14, about 11 or about 14.
- 25 15. The pharmaceutical composition of any one of claims 1 to 14, wherein the pharmaceutical composition comprises about 3 wt% to about 5 wt% of the compound having the general formula (A) or (A*) and about 95 wt% to about 97 wt% of the excipient, based on 100 wt% of the total pharmaceutical composition.

16. An oral dosage form comprising the pharmaceutical composition of any one of claims 1 to 15, the dosage form comprising about 1mg to about 100 mg of the compound, or about 5 mg to about 50 mg of the compound, preferably about 10 mg or about 30 mg of the compound.
- 5 17. The oral dosage form of claim 16, in the form of a capsule.
18. Use of the pharmaceutical composition of any one of claims 1 to 15 or the oral dosage form of claim 16 or 17, in the manufacture of a medicament for the treatment or prevention of a disease linked to protein aggregation and/or a neurodegenerative disease.
- 10 19. The use of claim 18, wherein the disease is an α -synucleinopathy.
20. The use of claim 19, wherein the synucleinopathy is multiple system atrophy (MSA), Parkinson's disease (PD), or dementia with Lewy bodies (DLB), preferably multiple system atrophy (MSA).
- 15 21. The use of any one of claims 18 to 20, wherein the pharmaceutical composition is to be administered orally and is to be administered to a subject without regard to food intake.
22. The pharmaceutical composition of any one of claims 1 to 15 or the oral dosage form of claim 16 or 17, for use in therapy.