wherein

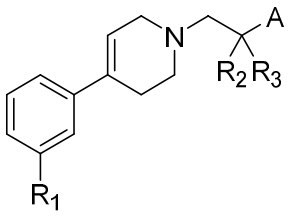
R_1 is a halogen atom, a CF_3 group, a $(C_1$-$C_4)$alkyl group or a $(C_1$-$C_4)$alkoxy group;

R_2 and R_3 are independently a hydrogen atom or a $(C_1$-$C_3)$alkyl group; and

A is:

- a phenyl radical substituted by a substituent X, wherein X is:
  - (a) a group selected from $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkylmethyl, $(C_3$-$C_6)$cycloalkoxy, $(C_3$-$C_6)$cycloalkylamino and cyclohexenyl; or
  - (b) a group selected from phenyl, phenylmethyl, phenylcarbonyl, phenoxy, phenylamino, N-$(C_1$-$C_3)$alkyl-phenylamino, phenylthio, phenylsulfinyl and phenylsulfonyl; or
- a 1-naphthyl or 2-naphthyl radical, either non-substituted or substituted in the 5-, 6-, 7- and/or 8-positions by one or two hydroxyl groups, one or two $(C_1$-$C_4)$alkoxy groups or a 6,7-methylenedioxy group.

[0007a] In one aspect, there is provided a use of a compound of formula (I) or a pharmaceutically acceptable salt and/or solvate thereof, in the manufacture of a medicament for the treatment of a hearing disease in a subject, wherein formula (I) is:



(I),

wherein

R_1 is a halogen atom, a CF_3 group, a $(C_1$-$C_4)$alkyl group or a $(C_1$-$C_4)$alkoxy group;

R_2 and R_3 are independently a hydrogen atom or a $(C_1$-$C_3)$alkyl group; and

A is:

- a phenyl radical substituted by a substituent X, wherein X is:
  - (a) a group selected from $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkylmethyl, $(C_3$-$C_6)$cycloalkoxy, $(C_3$-$C_6)$cycloalkylamino and cyclohexenyl; or

(b) a group selected from phenyl, phenylmethyl, phenylcarbonyl, phenoxy, phenylamino, N-(C_1-C_3)alkyl-phenylamino, phenylthio, phenylsulfinyl and phenylsulfonyl; or

- a 1-naphthyl or 2-naphthyl radical, either non-substituted or substituted in the 5-, 6-, 7- and/or 8-positions by one or two hydroxyl groups, one or two (C_1-C_4)alkoxy groups or a 6,7-methylenedioxy group.

[0008] Preferably, R_1 is a CF_3 group.

[0009] Preferably, at least one of R_2 and R_3 is a hydrogen atom, more preferably R_2 and R_3 are each a hydrogen atom.

[0010] Preferably, A is a biphenyl radical or a non-substituted 2-naphthyl radical.

[0011] Preferably, the salt is a hydrochloride salt or a fumarate salt of the compound of formula (I).

[0012] Advantageously, said compound is administered to the subject by oral route or by trans-tympanic route. More advantageously, said compound is administered to the subject by oral route or by trans-tympanic route, wherein the administration by trans-tympanic route consists in an injection between the eardrum and the round window by means of a needle which crosses the eardrum. Even more preferably, the compound is administered to the subject by trans-tympanic route, wherein the administration by trans-tympanic route consists in an injection between the eardrum and the round window by means of a needle which crosses the eardrum.

polyoxyethylated triglycerides and poloxamers, said pharmaceutical composition being a thermoreversible gel.

[0024] The present invention further relates to a pharmaceutical composition for use in the treatment of a hearing disease in a subject, said pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt and/or solvate thereof according to the invention, and at least one pharmaceutically acceptable excipient. Preferably, said hearing disease is as defined in the present description.

[0024a] In another aspect, there is provided a use of a pharmaceutical composition in the manufacture of a medicament for the treatment of a hearing disease in a subject, said pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt and/or solvate thereof as described herein and at least one pharmaceutically acceptable excipient, preferably said hearing disease being as defined herein.

DEFINITIONS

[0025] In the present invention, the following terms have the following meanings:

[0026] "**About**", before a figure or number, refers to plus or minus 10% of the face value of that figure or number. In one embodiment, "about", before a figure or number, refers to plus or minus 5% of the face value of that figure or number.

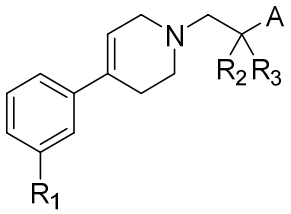
[0027] "**Active agent**" refers to an agent that has a therapeutic effect. The agent may be a chemical or a biological substance. Preferably, the active agent is a chemical substance. The therapeutic effect may be the prevention, delay, reduction in severity and/or frequency or suppression of at least one symptom associated with a pathological condition, or the prevention, slowing down or suppression of the underlying cause of a pathological condition, or the improvement or repair of a damage.

[0028] "**Alkyl**" by itself or as part of another substituent refers to a linear saturated hydrocarbyl group. Non-limiting examples of alkyl groups include methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, tert-pentyl, n-hexyl, iso-hexyl and tert-hexyl groups. Preferred alkyl groups include methyl,

ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl and tert-butyl groups. “**Cycloalkyl**” by itself or as part of another substituent refers to a cyclic saturated hydrocarbyl group. “**Alkoxy**” refers to -O-alkyl. “**Cycloalkoxy**” refers to -O-cycloalkyl. “**Cycloalkylamino**” refers to -NH-cycloalkyl.

CLAIMS

1. Use of a compound of formula (I) or a pharmaceutically acceptable salt and/or solvate thereof, in the manufacture of a medicament for the treatment of a hearing disease in a subject, wherein formula (I) is:



(I),

wherein

R_1 is a halogen atom, a CF_3 group, a (C_1-C_4)alkyl group or a (C_1-C_4)alkoxy group;

R_2 and R_3 are independently a hydrogen atom or a (C_1-C_3)alkyl group; and

A is:

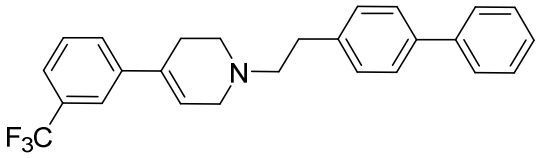
- a phenyl radical substituted by a substituent X, wherein X is:
  - (a) a group selected from (C_3-C_6)cycloalkyl, (C_3-C_6)cycloalkylmethyl, (C_3-C_6)cycloalkoxy, (C_3-C_6)cycloalkylamino and cyclohexenyl; or
  - (b) a group selected from phenyl, phenylmethyl, phenylcarbonyl, phenoxy, phenylamino, N-(C_1-C_3)alkyl-phenylamino, phenylthio, phenylsulfinyl and phenylsulfonyl; or
- a 1-naphthyl or 2-naphthyl radical, either non-substituted or substituted in the 5-, 6-, 7- and/or 8-positions by one or two hydroxyl groups, one or two (C_1-C_4)alkoxy groups or a 6,7-methylenedioxy group.

2. The use according to claim **1**, wherein R_1 is a CF_3 group.

3. The use according to claim **1** or **2**, wherein at least one of R_2 and R_3 is a hydrogen atom, preferably R_2 and R_3 are each a hydrogen atom.

4. The use according to any one of claims **1** to **3**, wherein A is a biphenyl radical or a non-substituted 2-naphthyl radical.

5. The use according to any one of claims **1** to **4**, wherein the compound of formula (I) is:



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6. The use according to any one of claims **1** to **5**, wherein the salt is a hydrochloride salt or a fumarate salt of the compound of formula (I).

7. The use according to any one of claims **1** to **6**, wherein said compound is to be administered to the subject by oral route or by trans-tympanic route, preferably said compound is to be administered to the subject by oral route or by trans-tympanic route wherein the administration by trans-tympanic route consists in an injection between the eardrum and the round window by means of a needle which crosses the eardrum, more preferably the compound is to be administered to the subject by trans-tympanic route wherein the administration by trans-tympanic route consists in an injection between the eardrum and the round window by means of a needle which crosses the eardrum.

8. The use according to any one of claims **1** to **7**, wherein said compound is to be administered by trans-tympanic route at a dose ranging from 10 µg to 400 mg, between once a month and once every 12 months, preferably said administration by trans-tympanic route consists in an injection between the eardrum and the round window by means of a needle which crosses the eardrum.

9. The use according to any one of claims **1** to **8**, wherein the hearing disease is selected from the group consisting of unilateral or bilateral hearing loss, unilateral or bilateral tinnitus, unilateral or bilateral hyperacusis, hidden hearing loss such as cochlear synaptopathy associated with a normal threshold, speech-intelligibility deficit, unilateral or bilateral temporary auditory threshold shift, central auditory processing disorder, unilateral or bilateral auditory recruitment, acoustic neuroma, single sided deafness, excitotoxicity, ototoxicity such as drug-induced ototoxicity and any combination thereof, preferably the hearing disease is selected from the group consisting of unilateral and

bilateral hearing loss such as a unilateral and bilateral sensorineural hearing loss, unilateral or bilateral tinnitus, unilateral or bilateral hyperacusis, hidden hearing loss such as cochlear synaptopathy associated with a normal threshold, and speech-intelligibility deficit.

10. The use according to any one of claims **1** to **9**, wherein the hearing disease is a unilateral or bilateral sensorineural hearing loss selected from the group consisting of unilateral or bilateral noise-induced sensorineural hearing loss, unilateral or bilateral inflammation-induced sensorineural hearing loss, unilateral or bilateral sudden idiopathic sensorineural hearing loss, unilateral or bilateral ototoxic chemicals-induced sensorineural hearing loss and unilateral or bilateral aged-induced sensorineural hearing loss such as presbycusis, preferably the hearing disease is a unilateral or bilateral sensorineural hearing loss selected from the group consisting of unilateral or bilateral noise-induced sensorineural hearing loss and unilateral or bilateral aged-induced sensorineural hearing loss.

11. The use according to any one of claims **1** to **10**, wherein the hearing disease is a unilateral or bilateral inflammation-induced sensorineural hearing loss caused by a chronic inflammatory disease, preferably said chronic inflammatory disease is selected from the group consisting of diabetes, chronic kidney disease, inflammatory bowel diseases and rheumatoid arthritis.

12. The use according to any one of claims **1** to **11**, wherein the hearing disease is a unilateral or bilateral hearing loss with a tonal audiometric threshold above 30 dB at 3 contiguous frequencies optionally associated with unilateral or bilateral tinnitus, preferably the hearing disease is a unilateral or bilateral hearing loss with a tonal audiometric threshold from 30 dB to 70 dB at 3 contiguous frequencies optionally associated with unilateral or bilateral tinnitus, the tonal audiometric threshold being measured by auditory brainstem response or pure-tone audiometry.

13. The use according to any one of claims **1** to **12**, wherein said subject is wearing at least one hearing device.

14. The use according to any one of claims **1** to **13**, wherein the compound of formula (I) or a pharmaceutically acceptable salt and/or solvate thereof is to be administered to the subject during a cochlear surgery, for example during a cochlear implant surgery.

15. The use according to any one of claims **1** to **14**, wherein said subject is a mammalian animal with an eardrum, preferably said mammalian animal with an eardrum is selected from the group consisting of a human, a cat, a dog and a non-human primate animal, more preferably said mammalian animal with an eardrum is a dog.

16. A pharmaceutical transtympanic composition comprising a compound of formula (I) or a pharmaceutically acceptable salt and/or solvate thereof as defined in any one of claims **1** to **6** and a combination of a mixture of polyoxyethylated triglycerides and poloxamers, said pharmaceutical composition being a thermoreversible gel.

17. Use of a pharmaceutical composition in the manufacture of a medicament for the treatment of a hearing disease in a subject, said pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt and/or solvate thereof as defined in any one of claims **1** to **6** and at least one pharmaceutically acceptable excipient, preferably said hearing disease being as defined in any one of claims **9** to **12**.