extract, raises the questions of the environmental and sustainable development as they contribute to the scarcity of fishery resources.

The glycerophospholipid vectors of omega -3 fatty acids developed are, for instance, phosphatidylserine vectors. A further one is a vector that mimics lysophosphatidylcholine for a particular family of omega-3 fatty acids including docosahexaenoic acid or DHA (WO 2018/162617). Although glycerophospholipid based vectors have a better cerebral targeting than ethyl and triglyceride form-based vectors, they have the inconvenience of being monovalent vectors of fatty acids (ex: docosahexanoic acid only), with short-term delivery only.

Thus, there is nowadays a strong need to develop new vector compounds that allow delivery of one or more active compounds, like fatty acids, in the acute (short term) and prolonged (long term) fashion, along the digestive tract, in order to provide effective treatments, not only in the cases of inflammation and epileptic seizures, but also in the preservation and/or restoration of cognitive functions associated or not with behavioral and/or psychoaffective disorders. Also, the development of fatty acid derivatives remains an important need in these applications.

SUMMARY

The inventors have developed a new family of molecular vectors and new active compounds, especially ethanolamine, ethanolamine-phosphonate or ethanolamine-phosphate derivative of saturated or unsaturated fatty acids. The active compounds have strong anti-inflammatory activity, and can decrease seizure severity and frequency and/or restore or improve cognitive functions, which may be altered in neurological disorders with a significant inflammatory component. The new family of molecular vectors includes two subfamilies, namely SphingoSynaptoLipoxins (SSLs) and AminoGlyceroPhosphoSynaptoLipoxins (AGPSLs).

In one aspect, the present disclosure relates to a compound of formula (IIA):

$$R_5\text{-NH-CH}_2\text{-CH}(R_7)\text{-PO}_3^{2-} \text{ (IIA)},$$

wherein:

- R_5 represents a saturated or unsaturated fatty acyl comprising from 2 to 30 carbon atoms selected in the group consisting of: propionic acid, butyric acid, valeric acid, caprylic acid, capric acid, lauric acid, myristic acid, stearic acid, arachidic acid, behenic acid,

lignoceric acid, myristoleic acid, palmitoleic acid, oleic acid, vaccenic acid, linoleic acid, alpha-linoleic acid, arachidonic acid, eicosapentaenoic acid, erucic acid, and docosahexaenoic acid, preferably capric acid, eicosapentaenoic acid, and docosahexaenoic acid or one of its oxygen derivatives chosen from resolvins, maresins, neuroprotectins, and neuroprostanes; and

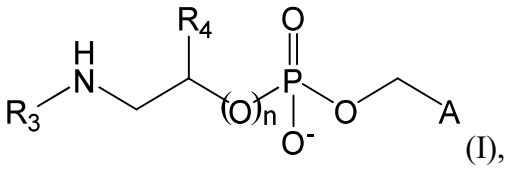
- R_7 represents a hydrogen or a (C_1-C_6)alkyl group;

and the hydrates, or the diastereoisomers, or the pharmacologically acceptable salts thereof.

In another aspect, the present disclosure relates to a compound as disclosed herein for use as a medicine. In another aspect, the present disclosure relates to a pharmaceutical composition comprising at least one compound as disclosed herein, and an acceptable pharmaceutical excipient.

In yet another aspect, the present disclosure relates to use of a pharmaceutical composition as disclosed herein, in the manufacture of a medicament for preventing and/or treating a disease chosen among an inflammatory disease or a ~~disease associated with a~~ cognitive disorder. In yet another aspect, the present disclosure relates to use of a pharmaceutical composition as disclosed herein, in the manufacture of a medicament for preventing and/or treating a disease selected in the group consisting of epilepsy, traumatic brain injury, Alzheimer's disease, Parkinson's disease, Multiple Sclerosis, Crohn's Disease, Bowel's Syndrome, Dementia, and Huntington's Disease. In yet another aspect, the present disclosure relates to use of a pharmaceutical composition as disclosed herein, in the manufacture of a medicament for preventing cognitive decline or restoring cognitive functions altered in brain injuries and/or in traumatic brain injuries and/or in a neuroinflammatory disease, and/or in a neurodegenerative disease.

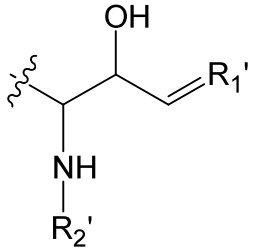
Accordingly, the present disclosure relates to a compound of formula (I):



(I),

in which:

- n is a whole number equal to 0 or 1;
- A represents a radical chosen among:
  - a group of formula (A'):



(A'),

CLAIMS

1. A compound of formula (IIA):

$$R_5\text{-}NH\text{-}CH_2\text{-}CH(R_7)\text{-}PO_3^{2-} \text{ (IIA)},$$

wherein:

- R_5 represents a saturated or unsaturated fatty acyl comprising from 2 to 30 carbon atoms selected in the group consisting of: propionic acid, butyric acid, valeric acid, caprylic acid, capric acid, lauric acid, myristic acid, stearic acid, arachidic acid, behenic acid, lignoceric acid, myristoleic acid, palmitoleic acid, oleic acid, vaccenic acid, linoleic acid, alpha-linoleic acid, arachidonic acid, eicosapentaenoic acid, erucic acid, and docosahexaenoic acid, preferably capric acid, eicosapentaenoic acid, and docosahexaenoic acid or one of its oxygen derivatives chosen from resolvins, maresins, neuroprotectins, and neuroprostanes; and
- R_7 represents a hydrogen or a (C_1-C_6)alkyl group;

and

the hydrates, or the diastereoisomers, or the pharmacologically acceptable salts thereof.

2. A compound according to claim 1, wherein:

- R_5 represents a saturated or unsaturated fatty acyl comprising from 2 to 30 carbon atoms, which is docosahexaenoic acid; and
- R_7 represents a hydrogen.

~~3. A compound according to claim 1, wherein R_5 represents:~~

~~- a saturated or unsaturated fatty acyl comprising from 2 to 30 carbon atoms selected in the group consisting of: acetic acid, propionic acid, butyric acid, valeric acid, caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, arachidic acid, behenic acid, lignoceric acid, myristoleic acid, palmitoleic acid, oleic acid, vaccenic acid, linoleic acid, alpha-linoleic acid, arachidonic acid, eicosapentaenoic acid, erucic acid, and docosahexaenoic acid, preferably capric acid, eicosapentaenoic acid, and docosahexanoic acid, or~~

~~- an oxygen derivative of a saturated or unsaturated fatty acyl comprising from 2 to 30 carbon atoms chosen from resolvins, maresins, neuroprotectins, and neuroprostanes.~~

~~4~~3. A compound according to ~~any one of~~ claim~~s~~ 1 ~~to 3~~or 2, for use as a medicine.

~~54~~. A pharmaceutical composition comprising at least one compound as defined in any one of claims 1 to 3, and an acceptable pharmaceutical excipient.

~~65~~. Use of a pharmaceutical composition as defined in claim ~~54~~, in the manufacture of a medicament for preventing and/or treating a disease chosen among an inflammatory disease or a ~~disease associated with a~~ cognitive disorder.

~~76~~. The use according to claim ~~65~~, wherein the inflammatory disease is an inflammatory disease of the central nervous system, an inflammatory disease of the digestive tract, an inflammatory joint disease, or an inflammatory disease of the retina.

~~87~~. Use of a pharmaceutical composition as defined in claim ~~54~~, in the manufacture of a medicament for preventing and/or treating a disease selected in the group consisting of epilepsy, traumatic brain injury, Alzheimer's disease, Parkinson's disease, Multiple Sclerosis, Crohn's Disease, Bowel's Syndrome, Dementia, and Huntington's Disease.

~~98~~. Use of a pharmaceutical composition as defined in claim ~~54~~, in the manufacture of a medicament for preventing cognitive decline or restoring cognitive functions altered in brain injuries and/or in traumatic brain injuries and/or in a neuroinflammatory disease, and/or in a neurodegenerative disease.

~~109~~. The use according to any one of claims ~~65~~ to ~~98~~, wherein said pharmaceutical composition is to be administered by oral route.