SYNTHETIC ANALOGUES OF 3-IODOTHYRONAMINE (T1AM) AND USES THEREOF

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PATENT STATUS: GRANTED

PRIORITY NUMBER: TO2014A000278

PRIORITY DATE: 03/04/2014

Invention

The invention aims to the development of new **synthetic analogs of 3-iodothyronamine (T1AM)**, an exponent of a class of **endogenous molecules derived from thyroid hormones.**

The possible main therapeutic uses are:

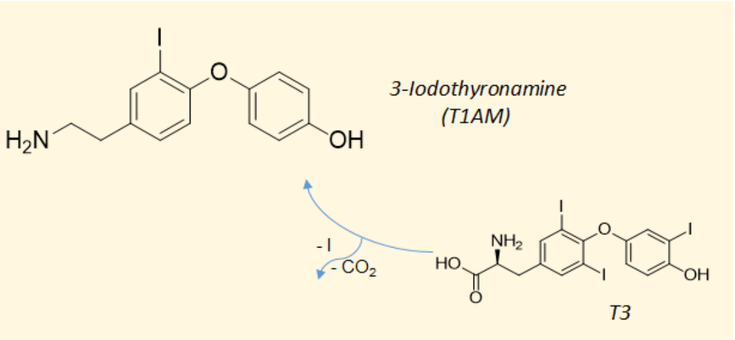
- treatment of obesity and dyslipidemia;
- neuro-psychiatric and behavioral disorders;
- neurodegenerative diseases (i.e. Alzheimer syndrome).

Numerous experimental evidences suggest the presence of a strong **correlation between obesity and neurodegeneration**. **Neurodegenerative diseases (NDDs)** are characterized by a progressive loss of memory and cognition, which can eventually lead to death. This deterioration is mainly due to inflammation triggered by aberrant protein deposition, oxidative stress, and modification of lipid pathways. These factors are closely related to obesity and overweight, thus correlating high adiposity with a risk factor for metabolic and neurodegenerative diseases [1]. In this context, the lipid-lowering and memory-enhancing effects, observed following the administration of these new molecules, suggest a novel pleiotropic therapeutic approach for the treatment of diseases such as obesity and NDD [2].

[1] *Journal of the Endocrine Society*, 4, Suppl_1, **020**, SUN-717, https://doi.org/10.1210/jendso/bvaa046.1733
[2] *Pharmaceuticals* **2021**, *14*(12), 1330; https://doi.org/10.3390/ph14121330

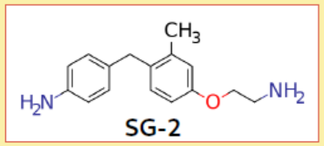
Drawings
& pictures

TIRONAMINE



AGONISTA ENDOGENO TAAR1

MESSAGGERO CHIMICO



- Promotes mnemonic & cogntive effects
- Prevents neuroinflammatory damage
- Promotes rebalancing of impaired autophagy

Possible tool for treatment of neurodegenerative disorders, such as AD and PD

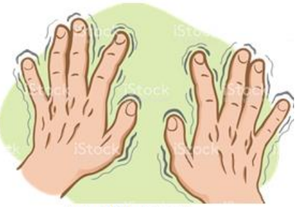
INTERAZIONE TAAR1 – T1AM → SVILUPPO NUOVI LIGANDI → NUOVE TERAPIE SNC


SCHIZOFRENIA


BIPOLARISMO

ADHD


ALZHEIMER


PARKINSON

Industrial applications

The proposed technology could contribute to the development of an innovative pharmaceutical approach for the treatment of:

- metabolic diseases, such as obesity, dyslipidemia and type II diabetes mellitus;
- cardiovascular and neurological diseases;
- aging-associated disorders.

BENEFITS

- The molecules are structurally novel;
- Newly synthesized molecules are metabolically more stable than endogenous analogs;
- They promote autophagic processes.

Possible developments

Current studies involve more than 30 molecules, that showed to be active in promoting autophagy in different cell lines. Cytotoxicity has been tested in 4 different cell lines. In collaboration with external institutions, studies are currently underway on cardiotoxicity by evaluating hERG channel inhibition, inhibition of certain cytochrome P450 isoforms, and off-target activities of molecules [2].

Further studies will focus on the screening of other structural analogs to understand their mechanism of action and evaluate their *in vitro* and *in vivo* efficacy.

The inventors are interested to undertake future collaborations to increase the technological readiness level of the invention and expand innovative drug opportunitis, considering eventual licensing or transferring to interested pharmaceutical companies.

[2] *Pharmaceuticals* **2021**, *14*(12), 1330; https://doi.org/10.3390/ph14121330

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