

COMPOUNDS FOR USE IN THE
THERAPEUTIC AND PREVENTIVE
TREATMENT OF
NEURODEGENERATIVE DISEASES,
PARTICULARLY ALZHEIMER'S
DISEASE



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Invention



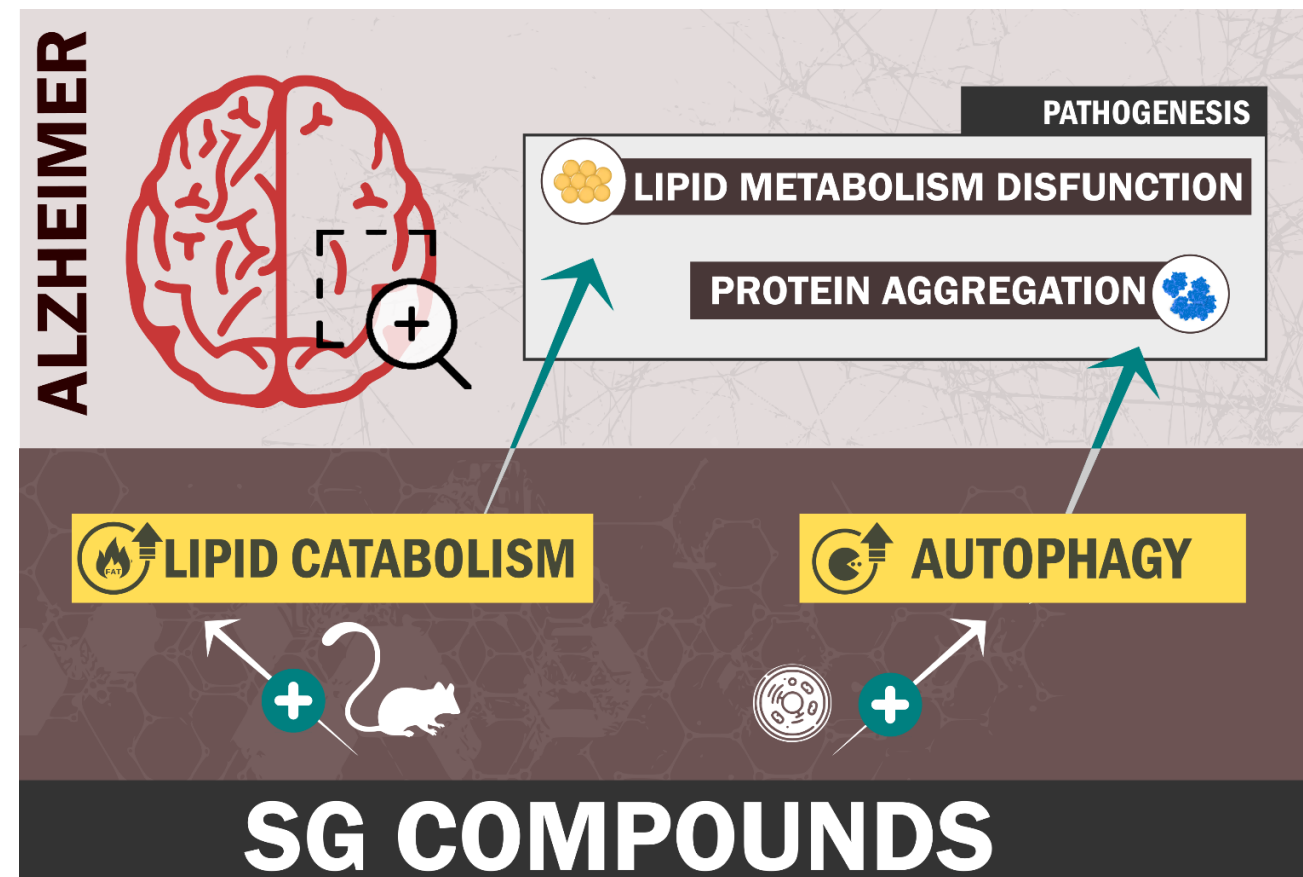
The object of the present invention is the design, synthesis, and pharmacological evaluation of **novel diphenylmethane core molecules**, capable of simultaneously promoting activation of the autophagy process and lipid catabolism, both *in vitro* and *in vivo*. Their dual activity may represent a novel approach for the **treatment of neurodegenerative diseases**, such as Alzheimer.

Neurodegenerative diseases are characterized by a progressive and irreversible loss of cognitive faculties, which can lead to death. This process is mainly due to **deposition of protein aggregates in nerve tissues** and **alterations in lipid metabolism**, which contribute to (a) a chronic state of inflammation and (b) hyperactivation of apoptotic processes at the expense of autophagy. Consequently, a new therapeutic approach could be the activation of lipid catabolism and simultaneously the promotion of autophagic process, which could promote the removal of toxic protein aggregates.

The new synthetic molecules promote both effects *in vitro* and *in vivo* in a pathological model of *C. elegans*, inducing a marked improvement in the clinical picture of Alzheimer's disease. Experiments on *C. elegans* nematodes confirmed the promising results obtained from the *in vitro* assays, setting up further tests for preclinical validation [1].

¹ *Pharmaceuticals* **2021**, 14(12), 1330; <https://doi.org/10.3390/ph14121330>

Drawings
& pictures



Molecules **2020**, *25*(5),
1054;
<https://doi.org/10.3390/molecules25051054>

SG
COMPOUNDS

LIPOLYTIC SAFE
PRO-AUTOPHAGIC

NEW
APPROACH
AGAINST
ALZHEIMER

Pharmaceuticals **2021**,
14(12), 1330;
<https://doi.org/10.3390/ph14121330>
Journal of the Endocrine Society, *4*, Suppl_1, **2020**,
SUN-717,
<https://doi.org/10.1210/je-ndso/bvaa046.1733>

SG-2
PROMOTES

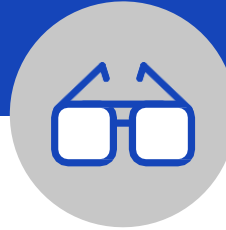
AUTOPHAGY
IN VITRO & IN VIVO

LIPID CATABOLISM
VIA AMPK ACTIVATION

LONGER LIFESPAN
IN NEMATODE MODEL OF AD

NEUROPROTECTION
IN VITRO & IN VIVO

Industrial applications



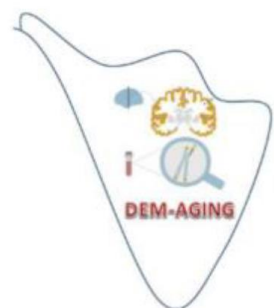
The invention is applicable to the pharmaceutical industry.

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

- **neurodegenerative diseases**, especially Alzheimer;
- **rare forms of dementia** (i.e. Neuronal Ceroid Lipofuscinosis, CLN).
- **metabolic diseases**.

The identification of a lead compound from the developed class of synthetic analogs could lead to the recognition of candidate first-in-class for the aforementioned pathologies.

The patented class of compounds is under investigation in two funded projects:



**Bando Ricerca Salute
2018 – Regione
Toscana DEM-AGING**



Insight CLN5: Approaching therapies in the neuronal ceroid lipofuscinosis, using Zebrafish as a Tool

Possible developments



Chemical-physical, biological and pharmacological characterization of more than 20 molecules is under investigation using original study models, already demonstrating low toxicity confirmed by ADME-T profiling.

The expected results of the studies aim to confirm the acquired data on the promotion of autophagy in different cell lines, understand the role of AMPK on the promotion of autophagy induced by the developed compounds, further investigate the activation of the autophagic process, and identify the specific molecular targets.

The wide range of active studies on various frontlines is possible through an extensive network of national and international collaborations with academic researchers and pharmaceutical companies. The inventors are looking for additional collaborations and licensing opportunities to increase the technological readiness of the invention and expand the supply of innovative drugs for the treatment of neurodegenerative diseases and metabolic disorders.

For more information:



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