



LICENSING OPPORTUNITY:

Phloretin: A natural approach to support nerve function/repair

BACKGROUND INFORMATION

Flavonoids, abundantly present in fruit and vegetables, form one of the largest phytonutrient families with diverse biochemical properties. The best-described bioactivities of these flavonoids include anti-inflammatory and anti-oxidative effects.

In particular, the flavonoid **phloretin**, which can be found in apples and strawberries, is known for its immunomodulatory features and is widely used for skincare due to its anti-oxidative characteristic.

Hasselt University has shown that phloretin plays a crucial role in nerve repair, by **decreasing neuroinflammation** and **promoting remyelination**, hereby having a positive effect on **neurological functioning**. This is of interest to limit neuronal loss in neurodegenerative and demyelinating diseases such as multiple sclerosis (MS), where therapeutics that influence both immune and repair processes are currently still lacking.



UHASSELT

KNOWLEDGE IN ACTION

COMPELLING RESULTS

Hasselt University tested a range of natural compounds in their **Nutriscreen Platform**. This platform consists of *in vitro*, *in vivo* and **ex vivo** models for neuroinflammation and CNS repair.

Phloretin suppresses the inflammatory phenotype of macrophages and reduces **neuroinflammation** in an animal model. Moreover, our findings demonstrate that phloretin also markedly stimulates *ex vivo* and *in vivo* **remyelination**. Improved remyelination was attributed to a direct impact of phloretin on oligodendrocyte precursor cell (OPC) maturation.

These findings support the use of phloretin for the **improvement of neurological functioning**.

Since phloretin affects both the immunomodulatory and neurodegenerative aspect, it holds **potential as a natural add-on therapy** of this demyelinating disorders, such as MS.

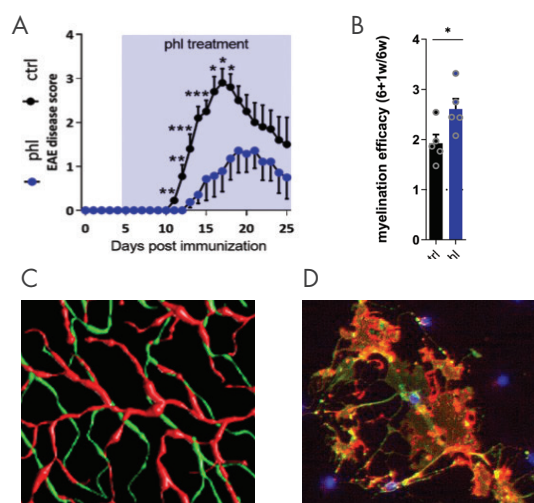


Figure 4: A; Influence of phloretin treatment (ip) on disease symptoms in an animal model for neuroinflammation. Mice are immunized with a myelin peptide in combination with adjuvants. Animals become paralysed after 10 days (1= partial paralysis, 4= full paralysis). Phloretin treatment significantly improves the paralysed phenotype. B. Addition of cuprizone to the diet leads to demyelination in the brains of mice. Withdrawal of cuprizone leads to repair (remyelination) which is enhanced by phloretin treatment (IP). C Remyelination (red) of neurons (green) after induction of demyelination in mouse brain slices is enhanced by phloretin. D. Oligodendrocyte precursor cells differentiate into myelinating oligodendrocytes after the addition of phloretin.

KEY FEATURES AND ADVANTAGES

- **Natural** component, present in fruit
- Possible application in **pharmaceutical** and **food** or **nutraceutical** market
- Suppression of **neuroinflammation** in an animal model of Multiple Sclerosis.
- Stimulation of **myelin repair** in brain slice cultures and an animal model of MS.
- Therapeutics that target **both** immune and repair processes are lacking.
- Improving physical and/or cognitive ability, fatigue and or in **improving neurological functioning**.
- Clinical applications include neurodegenerative and demyelinating diseases (e.g. progressive MS, diabetic neuropathy, Marie-Charcot tooth disease or traumatic nerve injury, chronic inflammatory polyradiculoneuropathy, Guillain Barre syndrome.)

MARKET POTENTIAL

With \$725bn of global sales in 2018, and \$764 bn in 2020, Health and Wellness is a large and significant component of the global Food and Beverage market. The growing awareness of the influence of food on health is one of the driving factors for this market.

In addition the demyelinating diseases therapeutic market is growing, with the global MS market expected to reach 25 billion USD in the next 5 years. Current blockbuster drugs (e.g. Ocrevus) achieve annual global sales of over 5 billion USD

OUTSTANDING OPPORTUNITY

Patent application is available for licensing.

UHasselt is searching interested parties to complete development and commercialization.

RELEVANT PUBLICATIONS

Dierckx T, Haidar M, Grajchen E, Wouters E, Vanherle S, Loix M, Boeykens A, Bylemans D, Hardonnière K, Kerdine-Römer S, Bogie JFJ, Hendriks JJA. Phloretin suppresses neuroinflammation by autophagy-mediated Nrf2 activation in macrophages. *J Neuroinflammation*. 2021 Jul 4;18(1):148. doi: 10.1186/s12974-021-02194-z.

Dierckx T, Vanherle S, Haidar M, Grajchen E, Mingneau F, Gervois P, Wolfs E, Bylemans D, Voet A, Nguyen T, Hamad I, Kleinewietfeld M, Bogie JFJ, Hendriks JJA. Phloretin enhances remyelination by stimulating oligodendrocyte precursor cell differentiation. *Proc Natl Acad Sci U S A*. 2022 Nov 16;119(46):e2120393119. doi: 10.1073/pnas.2120393119

BUSINESS DEVELOPER

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