Dipartimento di Farmacia

Università degli Studi di Napoli Federico II

Tutor: Angela Corvino

Co-tutor: Ferdinando Fiorino

PROJECT TITLE Development of Multi-target nutraceutical-H_2S donor hybrids for the modulation of neuroinflammation in neurodegenerative diseases.

Project description (max 300 words**)**

Neuroinflammation is a key pathological hallmark of major neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis [1]. Chronic activation of microglia and astrocytes promotes the release of pro-inflammatory mediators, oxidative stress and mitochondrial dysfunction, contributing to progressive neuronal damage and disease progression [2].
Since current therapies are mainly symptomatic and target single pathways, innovative multi-target approaches are needed to address the complex mechanisms underlying neurodegeneration.
Among the endogenous mechanisms involved in the maintenance of neuronal homeostasis, hydrogen sulfide (H_2S) has recently emerged as a crucial gasotransmitter in the central nervous system. Beyond its physiological neuromodulatory functions, H_2S plays a pivotal role in controlling neuroinflammation, oxidative stress and mitochondrial integrity through the modulation of signaling pathways such as Nrf2, NF-κB and NLRP3 [3]. Reduced H_2S bioavailability has been associated with several neurodegenerative conditions, suggesting that H_2S-releasing molecules may represent a promising therapeutic strategy for restoring cellular homeostasis and counteracting neuroinflammatory processes.
In parallel, increasing attention has been devoted to bioactive compounds derived from characteristic components of the Mediterranean diet, including cruciferous vegetables, rosemary and sage, which are rich in phytochemicals with well-documented antioxidant, anti-inflammatory and neuroprotective properties [4-5].
The proposed research aims to develop a novel class of multi-target hybrid molecules combining Mediterranean diet-derived bioactives with natural or synthetic H_2S donors. The resulting hybrids are expected to simultaneously modulate multiple pathogenic mechanisms involved in neurodegeneration, including oxidative stress, microglial activation, inflammasome signaling and neuronal dysfunction.
The compounds will be evaluated in cellular models of neuroinflammation using microglial and neuronal cell lines exposed to inflammatory stimuli. Their effects on cytokine production, oxidative stress, Nrf2 activation, inflammasome modulation and neuronal survival will be investigated.

REFERENCES

[1] Fołta, J.; Rzepka, Z.; Wrześniok, D. The Role of Inflammation in Neurodegenerative Diseases: Parkinson's Disease, Alzheimer's Disease, and Multiple Sclerosis. *Int. J. Mol. Sci.* **2025**, *26*, 5177. https://doi.org/10.3390/ijms26115177.

Dipartimento di Farmacia
Via Domenico Montesano, 49 • 80131 Napoli, Italia
nomecognome@unina.it • + 39 081678658
www.farmacia.unina.it

[2] Dash UC, Bhol NK, Swain SK, Samal RR, Nayak PK, Raina V, Panda SK, Kerry RG, Duttaroy AK, Jena AB. Oxidative stress and inflammation in the pathogenesis of neurological disorders: Mechanisms and implications. Acta Pharm Sin B. 2025; 15(1):15-34. doi: 10.1016/j.apsb.2024.10.004.

[3] Zhang Y, Zhang Q, Yang L, Fan Y, Zheng P, Liu T, Gao X, Ren Z, Wang X, Zhou B, Liu W, Xin T, Tang L, Han M. Hydrogen Sulfide: A Multitarget Therapeutic for Neuroinflammation in Neurodegenerative Diseases. Research (Wash DC), 2026, 9:1107. doi: 10.34133/research.1107.

[4] Faridzadeh A, Salimi Y, Ghasemirad H, Kargar M, Rashtchian A, Mahmoudvand G, Karimi MA, Zerangian N, Jahani N, Masoudi A, Sadeghian Dastjerdi B, Salavatizadeh M, Sadeghsalehi H, Deravi N. Neuroprotective Potential of Aromatic Herbs: Rosemary, Sage, and Lavender. Front Neurosci. 2022 Jun 28;16:909833. doi: 10.3389/fnins.2022.909833.

[5] Kakarla R, Karuturi P, Siakabinga Q, Kasi Viswanath M, Dumala N, Guntupalli C, Nalluri BN, Venkateswarlu K, Prasanna VS, Gutti G, Yadagiri G, Gujjari L. Current understanding and future directions of cruciferous vegetables and their phytochemicals to combat neurological diseases. Phytother Res. 2024 Mar;38(3):1381-1399. doi: 10.1002/ptr.8122.