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Purple Corn Anthocyanins Protect against the Progression of Multiple Sclerosis-Associated Trigeminal Pain

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Benedetta Riboldi [1], Giulia Magni [2], Alessandra Marinelli [3], Fabrizia Bonacina [2], Patrizia Uboldi [2], Katia Petroni [3], Stefania Ceruti [4]

1. Department of Pharmacological and Biomolecular Sciences “Rodolfo Paoletti”, Università degli Studi di Milano, MIlano, ITA 2. Department of Pharmacological and Biomolecular Sciences “Rodolfo Paoletti”, Università degli Studi di Milano, Milano, ITA 3. Department of Biosciences, Università degli Studi di Milano, Milano, ITA 4. Department of Pharmacological and Biomolecular Sciences “Rodolfo Paoletti”, Università degli Studi di Milan, Milano, ITA

Corresponding author: Benedetta Riboldi, benedetta.riboldi@unimi.it

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Abstract

Pain is one of the most disabling symptoms of multiple sclerosis (MS) [1]. Trigeminal (TG) neuralgia and migraine often precede MS diagnosis, don’t correlate with disease severity [2], and are often insensitive to classic analgesics, requiring the use of other drugs with severe side effects [3]. Thus, new approaches based on nutraceutical supplements enriched in molecules with pharmacological activities could be a winning strategy. Anthocyanins (ACNs) can prevent chronic diseases through antioxidant, anti-inflammatory, and neuroprotective effects [4]. Our group already demonstrated the anti-allodynic effect of ACNs in a rat model of TG sensitization, through inhibition of microgliosis and production of anti-inflammatory mediators [5]. Here, we aimed to verify if ACN-enriched purple corn exerts beneficial effects on the onset and progression of MS-associated TG pain.

Relapsing-remitting experimental autoimmune encephalomyelitis (EAE) was induced in male Dark Agouti rats via immunization with MOG_{1-125} peptide [6]. Eleven days before, rats were assigned to drink water, yellow corn (containing all classes of flavonoids except for ACNs) as control, or purple corn extracts as a preventive approach. Another group of animals began drinking purple corn extract from the onset of EAE motor symptoms, as a therapeutic strategy. Rats were weighed daily, the development of EAE was evaluated by a scale of ascending paralysis, and spontaneous TG pain was measured by von Frey test. After sacrifice at day post-immunization 21, CNS tissues were collected for subsequent analyses.

Preventive purple corn administration: 1) delays and reduces the development of EAE-associated TG pain; 2) facilitates the remission of EAE motor symptoms and protects against the development of relapses; 3) limits glial cell activation; 4) ameliorates the ratio between anti- and pro-inflammatory mediators; 5) activates autophagy; 6) reduces immune cells infiltration in the brainstem (BS) and lumbar spinal cord (LSC). Therapeutic purple corn administration does not affect EAE motor symptoms, only partially reduces the development of TG pain but maintains its ability to blunt neuroinflammation. Moreover, it is only partially effective in reducing immune cell infiltration in the BS and completely loses its effect in the LSC.

We show that the reduction of neuroinflammation could be one of the mechanisms underlying the protective effect of ACN preventive administration against the development of EAE-associated TG pain and motor relapses. Conversely, the partial efficacy of their therapeutic administration could rely upon the different ability to reduce immune cell infiltration in the BS and LSC with respect to the preventive administration. Further analyses are needed to set up a more effective therapeutic protocol of purple corn administration, which could be later translated from the preclinical stage to MS patients, also in combination with current analgesics to reduce their dosages and side effects.

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