



## Dimethyl fumarate alleviates the Nitroglycerin (NTG)-induced Migraine in Mice

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### Abstract

Oxidative stress and inflammatory pathways are involved in migraine and endogenous antioxidant defense system has a role in the prevention of hyperalgesia in migraine. In this study, we aimed to evaluate the role of the most pharmacologically effective molecules among the fumaric acid esters (FAEs), dimethyl fumarate, nuclear factor E2-related factor 2/antioxidant response element (Nrf2/ARE) pathway-mediated, in regulating the hypersensitivity in a mouse model of nitroglycerine (NTG)-induced migraine. Mice were orally administered with DMF at the doses of 10, 30 and 100 mg/kg, 5 minutes after NTG intraperitoneal injections. We performed histological and molecular analysis on the whole brain and behavioral tests after 4 h by NTG-migraine induction. Moreover, we evaluate Nrf-2 dependent mechanism by the in vitro stimulation of cells extracted by trigeminal ganglia with Diethylenetriamine/ nitric oxide (DETA/NO), a nitric oxide (NO) donor. The cell was pre-treated with DMF and an antagonist of Nrf-2, trigonelline (TR) 2h before DETA/NO stimulation. DMF treatment notably reduced histological damage as showed by cresyl violet staining; also, regulating both NF- $\kappa$ B and Nrf-2 pathway, DMF treatment decreased the severity of inflammation and increased the protective antioxidant action. Moreover, the headache, evaluated through behavioral tests, was significantly reduced. The protective effect of DMF treatment, via Nrf-2, were confirmed in in vitro studies, through inhibition of Nrf-2 by trigonelline. Cytotoxicity, iNOS and MnSOD expression were evaluated. These results provided the evidence that DMF, by Nrf-2 modulation, has a protective effect on central sensitization induced by NTG, suggesting a new insight into the potential application of DMF as novel candidates in drug development for migraine.

### Biography

Emanuela Esposito is working as professor in University of Messina, Italy. She has published, in this field, more than 50 papers, in many journals, many with Impact Factor.

### Publication:

The role of nitric oxide synthases in lung inflammation., Esposito E, Cuzzocrea S.

Peroxisome proliferator-activated receptors and shock state, Esposito E, Cuzzocrea S, Meli R

Proinflammatory role of glucocorticoid-induced TNF receptor-related gene in acute lung inflammation, Cuzzocrea S, Nocentini G, Di Paola R, Agostini M, Mazzon E, Ronchetti S, Crisafulli C, Esposito E, Caputi AP, Riccardi C



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