

## Product Data Sheet

Product Name: Dimethyl Fumarate

Cat. No.: GC16590

### Chemical Properties

Cas. No. 624-49-7

Chemical Name dimethyl (E)-but-2-enedioate

SMILES COC(=O)C=CC(=O)OC

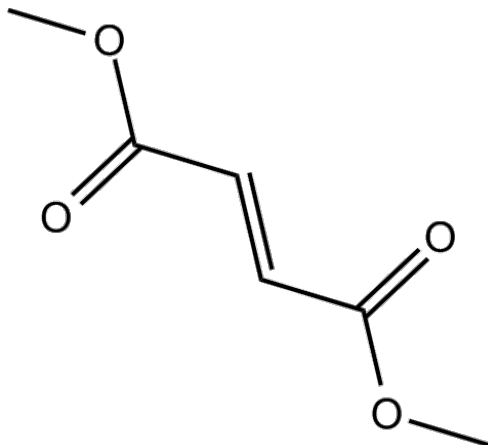
Formula C6H8O4 M.Wt 144.13

Solubility  $\geq 7.1\text{mg/mL}$  in DMSO Storage Store at RT

General tips For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



### Protocol

**Caution: Product has not been fully validated for medical applications. For research use only.**

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**Animal  
experiment:**

In a blinded design, the rats are assigned to one of the three experimental groups: a) to the DMF group receiving 10 mg/kg body weight DMF (dissolved in DMSO 2% in water), or b) to the vehicle group receiving only the vehicle (DMSO 2% in water; necessary to dissolve DMF), or c) to the positive control group receiving the vehicle plus ischemic preconditioning (IPC, known to reduce infarct size). This dose of 10 mg/kg body weight of DMF corresponded approximately to a maximally tolerated dose in man. As we could confirm in our in vitro experiments that DMF is the active compound, the in vivo experiments are performed with DMF but not with MHF. DMF and the vehicle, respectively, tail vein is administrated by i.v. 90 min before ischemia (under general anesthesia using isoflurane) as well as immediately before ischemia. Ischemic preconditioning is induced by two times 5 min episodes ischemia (induced by left coronary artery occlusion) each followed by 5 min of reperfusion (induced by releasing the snare). The experiments are performed (except pilot experiments) pair wise, i.e. two experiments in parallel avoiding identical group assignment. The present study are set up, and permitted to demonstrate a pharmacodynamic effect of DMF on myocardial infarct size in rats in vivo. An eventual mode of action should be investigated in vitro. The results from our in vitro experiments as well as results of other laboratories did not show any effect of MHF on NF- $\kappa$ B activation. Therefore, no experiment is included to exclude MHF from the mode of action of DMF.

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### References:

- [1]. Albrecht P, et al. Effects of dimethyl fumarate on neuroprotection and immunomodulation. J Neuroinflammation. 2012 Jul 7;9:163
- [2]. Peng H, et al. Dimethyl fumarate inhibits dendritic cell maturation via nuclear factor  $\kappa$ B (NF- $\kappa$ B) and extracellular signal-regulated kinase 1 and 2 (ERK1/2) and mitogen stress-activated kinase 1 (MSK1) signaling. J Biol Chem. 2012 Aug 10;287(33):28017-26.
- [3]. Meili-Butz S, et al. Dimethyl fumarate, a small molecule drug for psoriasis, inhibits Nuclear Factor- $\kappa$ B and reduces myocardial infarct size in rats. Eur J Pharmacol. 2008 May 31;586(1-3):251-8.
- [4]. Cross SA, et al. Dimethyl fumarate, an immune modulator and inducer of the antioxidant response, suppresses HIV replication and macrophage-mediated neurotoxicity: a novel candidate for HIV neuroprotection. J Immunol. 2011 Nov 15;187(10):5015-25.
- [5]. Jing X, et al. Dimethyl fumarate attenuates 6-OHDA-induced neurotoxicity in SH-SY5Y cells and in animal model of Parkinson's disease by enhancing Nrf2 activity. Neuroscience. 2015 Feb 12;286:131-40
- [6]. Li Y, et al. Dimethyl fumarate accelerates wound healing under diabetic condition. J Mol Endocrinol. 2018 Jul 23. pii: JME-18-0102.

### Background

Dimethyl fumarate is a nuclear factor (erythroid-derived)-like 2 (Nrf2) pathway activator and induces upregulation of antioxidant gene expression.

Dimethyl fumarate causes short-lived oxidative stress, which leads to increased levels and nuclear localization of the transcription factor nuclear factor erythroid 2-related factor 2 and a subsequent increase in glutathione synthesis and recycling in neuronal cells[1]. Dimethyl fumarate inhibits dendritic cell (DC) maturation by reducing inflammatory cytokine production (IL-12 and IL-6) and the expression of MHC class II, CD80, and CD86. Dimethyl fumarate impairs nuclear factor  $\kappa$ B (NF- $\kappa$ B) signaling via reduced p65 nuclear translocation and phosphorylation. Dimethyl fumarate inhibits maturation of DCs and subsequently Th1 and Th17 cell differentiation by suppression of both NF- $\kappa$ B and ERK1/2-MSK1 signaling[2]. Dimethyl fumarate inhibits TNF- $\alpha$ -induced nuclear entry of NF- $\kappa$ B in rat heart endothelial cells (RHEC)[3]. Dimethyl fumarate, an immune modulator and inducer of the antioxidant response, suppresses HIV replication and neurotoxin release. Dimethyl

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fumarate attenuates CCL2-induced monocyte chemotaxis, suggesting that Dimethyl fumarate could decrease recruitment of activated monocytes to the CNS in response to inflammatory mediators[4].

Dimethyl fumarate inhibits nuclear entry of NF-kappaB in RHEC and reduces myocardial infarct size after ischemia and reperfusion in rats in vivo[3]. Dimethyl fumarate oral administration is shown to upregulate mRNA and protein levels of Nrf2 and Nrf2-regulated cytoprotective genes, attenuate 6-OHDA induced striatal oxidative stress and inflammation in C57BL/6 mice[5].

### References:

- [1]. Albrecht P, et al. Effects of dimethyl fumarate on neuroprotection and immunomodulation. J Neuroinflammation. 2012 Jul 7;9:163
- [2]. Peng H, et al. Dimethyl fumarate inhibits dendritic cell maturation via nuclear factor  $\kappa$ B (NF- $\kappa$ B) and extracellular signal-regulated kinase 1 and 2 (ERK1/2) and mitogen stress-activated kinase 1 (MSK1) signaling. J Biol Chem. 2012 Aug 10;287(33):28017-26.
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