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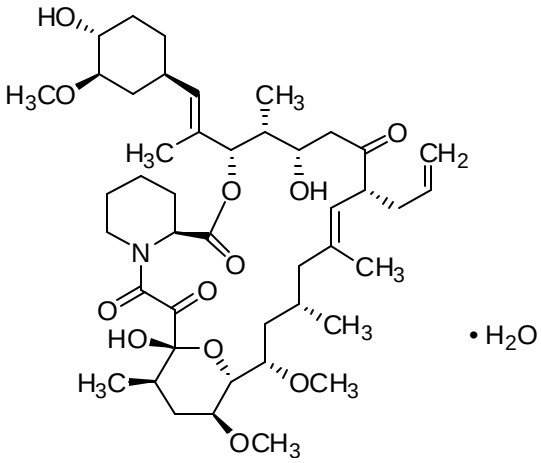
ProductInformation

FK-506 monohydrate

Catalog Number **F4679**
Storage Temperature –20 °C

CAS RN 109581-93-3
Synonym: Tacrolimus



Product Description

Molecular Formula: $C_{44}H_{69}NO_{12} \cdot H_2O$
Molecular Weight: 822.03

FK-506 is a potent immunosuppressant and *in vitro* T cell proliferation blocker. It has been shown to disrupt calcineurin (also known as CaN or phosphatase 2B) mediated signal transduction in T lymphocytes. The compound interacts with the FK-506-binding protein-12 (FKBP12). The resulting complex, in turn, interferes with calcineurin substrate interaction. FK-506 inhibits FKBP12 activity resulting in an increase in the release of sarcoplasmic reticulum-derived calcium. FK-506 also appears to inhibit Na^+/Ca^{2+} exchange. Prolonged exposure of *Xenopus* A6 cells to FK-506 significantly inhibits aldosterone-stimulated Na^+ transport and Na^+/K^+ ATPase activity. FKBP12, with or without bound FK506, has no effect on rat brain PKC activity *in vitro*. However, rapamycin plus FKBP12 does inhibit PKC activity.[1,2]

Neuroimmunophilin ligands are a class of compounds that may be applied for the treatment of nerve injuries and neurological diseases. In contrast to neurotrophins (e.g., nerve growth factor), these compounds readily cross the blood-brain barrier and are orally effective in a variety of animal models of ischemia, traumatic nerve injury, and human neurodegenerative disorders. Two ligands (cyclosporin A and FK-506) have already been used in humans as immunosuppressant drugs. Whereas, both cyclosporin A and FK-506 demonstrate neuroprotective actions, only FK-506 and its derivatives have significant neuroregenerative activity. The neuroprotective and neuroregenerative properties seem to arise via different mechanisms. The neuro-regenerative property does not involve calcineurin inhibition, essential for immunosuppression. This is important since most of the limiting side effects produced by these drugs arise via calcineurin inhibition. The ability to separate the neuroregenerative property of FK-506 from its immunosuppressant action via the development of non-immunosuppressant (non-calcineurin inhibiting) derivatives is essential.[3-5]

Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Preparation Instructions

Soluble in DMSO at >3 mg/mL

Storage/Stability

Store the product at –20 °C.

References

1. Rokaw, M.D., *et al*., FK-506 and rapamycin but not cyclosporin inhibit aldosterone-stimulated sodium transport in A6 cells. Am. J. Physiol., **271,** C194-202 (1996).
2. Rokaw, M.D., *et al*., Rapamycin inhibits protein kinase C activity and stimulates Na^+ transport in A6 cells, J. Biol. Chem. **271,** 32468-32473 (1996).
3. Gold, B.G., et al., Neuroregenerative and neuroprotective actions of neuroimmunophilin compounds in traumatic and inflammatory neuropathies. Neurol. Res., **26**, 371-380 (2004).
4. Gold, B.G., Neuroimmunophilin ligands: evaluation of their therapeutic potential for the treatment of neurological disorders. Expert Opin. Investig. Drugs, **9**, 2331-2342 (2000).
5. Dumont, F.J., FK506, an immunosuppressant targeting calcineurin function. Curr. Med. Chem. **7**, 731-748 (2000).

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