

# Specified Path CMC LEAD AND LINE PRODUCT DATE SHEET

issue date 01/06/2020

Product Name: Cyclosporin H, EvoPure®

Product Number: C046

**CAS Number:** 83602-39-5

Molecular Formula:  $C_{62}H_{111}N_{11}O_{12}$ 

Molecular Weight: 1202.6 g/mol

Form: Powder

**Appearance:** White crystal powder

Source: Tolypocladium Inflatum

**Water Content (Karl** 

Fischer):

3.0%

Melting Point: 162-165°C

Storage Conditions: -20°C

**Description:** Cyclosporin H is a hydroxylated metabolite of Cyclosporin A. Cyclosporin H

(M-1) and other cyclosporin metabolites have been found to have lower (<10%) immunosuppressant activity than cyclosporin A. Cyclosporin H has been found to be a potent inhibitor of superoxide anion (O<sub>2</sub>-) formation by FMLP (N-Formylmethionyl-leucyl-phenylalanine) in human neutrophils.

For more Cyclosporin products, click here.

**Mechanism of Action:** Cyclosporin H (and other cyclosporin A metabolites) have lower

immunosuppressant activity but most likely operate under the same

mechanism as cyclosporin A (CsA) described below.

Cyclosporin B (and other cyclosporin A metabolites) have lower

immunosuppressive activity but likely operate under the same mechanism as

cyclosporin A described below. After entering a T-cell, Cyclosporin A

associates with the cytosolic protein cyclophilin which helps in protein folding. Cyclosporin A binds to cyclophilins and this complex binds another cytosolic protein phosphatase called Calcineurin (protein phosphatase 2B) that dephosphorylates a transcription factor (nuclear factor of activated T-cells, or NF-AT) needed for expression of interleukin 2 (IL-2.). It also blocks the

pathway to nitric oxide synthesis via tumor necrosis factor (TNFa) and

Interleukin 1a.

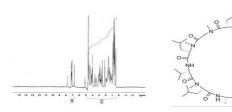
**Cancer Applications** Cyclosporin's immunosuppressive properties and potential toxicity can be

studied during in vitro assays. Other metabolites of Cyclosporin A (AM1, AM1c, DihydroAM1, AM19, and AM4N) can also be studied (Vollenbroeker B

et al, 2005).

#### **Technical Data:**

#### **HNMR Spectra**



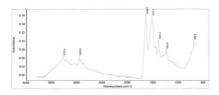
## Click to enlarge

Solvent: CDC13

Instrument: Mercury 300

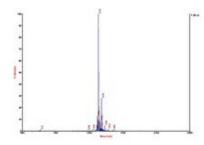
Frequency: 300 MHz

## **FTIR Spectra**



Click to enlarge

## **Mass Spectra**



#### Click to enlarge

Polarity/Scan Type: Positive
Solvent: MeOH

Solution Concentration: 0.1 mg/mL

**Instrument:** Agilent

#### References:

Anderson MA and Gusella JF (1984) Use of Cyclosporin A in establishing Epstein-Barr virus-transformed human lymphoblastoid cell lines. In Vitro 20(11):856-858. PMID 6519667

Copelan KR, Yatscoff RW and McKenna RM (1990) Immunosuppressive activity of Cyclosporine metabolites compared and characterized by mass spectrometry and nuclear magnetic resonance. Clin. Chem. 36(2): 225-229. PMID 2137384

Dreyfuss, M et al (1976) Cyclosporin A and C. Eur. J. Appl Microbiol. 3(2): 125-133

Laupacis A et al. PA (1982) Cyclosporin A: A powerful immunosuppressant. Can. Med Assoc. J 126(9):1041-1046 PMID 7074504

Matsuda S and Koyasu S (2000) Mechanisms of Action of Cyclosporine. Immunopharmacol. 47(2-3): 119-125. PMID 10878286

Matsuda, S (2000) Mechanisms of action of cyclosporine. Immunopharmacol. 47(2-3):119-125. PMID 10878286

Oliyai R. & Stella V. J. (1992) Kinetics and mechanism of isomerization of cyclosporin A. Pharm. Res. 9(5):617-622

Stiller, CR and Ulan RA (1981) Cyclosporin A: A Powerful Immunosuppressant."Can. Med. Assn. 126 (1981): 1041-046.

Vollenbroeker B et al (2005) Determination of cyclosporine and its metabolites in blood via HPLC-MS and correlation to clinically important parameters. Transplant Proc. 37(4):1741-1744 PMID 15919451

Wang, PC et al. (1989) Isolation of 10 Cyclosporine Metabolites from Human Bile. Drug Metab. Dispos. 17(3): 292-296 PMID 2568911

Watashi K, Hijikata M, Hosaka M, Yamaji M, Shimotohno K (2003) Cyclosporin A suppresses replication of hepatitis C virus genome in cultured hepatocytes. Hepatol. 38(5):1282-1288. PMID 14578868

Zheng XS, Chan T, and Zhou HH (2004) Genetic and genomic approaches to identify and study the targets of bioactive small molecules. Chem and Biol 11(5):609-618 PMID 15157872

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