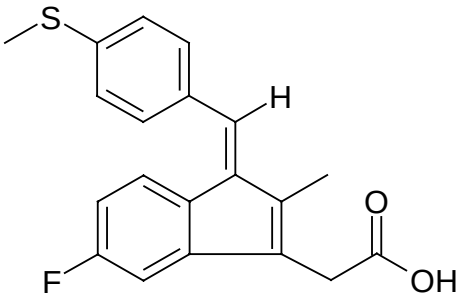
ProductInformation

SULINDAC SULFIDE
Product Number **S3131**
Storage Temperature: Room Temperature

CAS#: 32004-67-4
Synonym: (Z)-5-Fluoro-2-methyl-1-[p-(methylthio)benzylidene]indene-3-acetic acid



Product Description

Molecular Formula: $C_{20}H_{17}FO_2S$
Molecular Weight: 340.02 (anhydrous)

The small guanine-nucleotide binding-protein Ras participates in diverse processes including differentiation, cell proliferation, transformation and apoptosis (1). Ras is localized in the plasma membrane and can exist in two conformations: a guanosine triphosphate (GTP)-bound active state and the guanosine diphosphate (GDP)-bound inactive state. The GTP-bound form of Ras signals by preferentially binding to several effector molecules, most notably the serine-threonine kinase, c-Raf-1. Upon activation Raf-1 initiates a kinase cascade through MEK (mitogen-activated protein kinase kinase or ERK kinase), a dual-specificity protein kinase, that in turn phosphorylates ERK (extracellular signal-regulated kinase), another serine-threonine kinase. ERK, in turn, can phosphorylate other kinases, such as Rsk2 and/or transcription factors such as c-Fos (1,2).

Sulindac sulfide inhibits Ras activation of Raf-1 (3). *In vitro* studies show that sulindac sulfide non-covalently binds directly to the Ras gene product p21ras (3). Sulindac sulfide has also been shown to impair nucleotide exchange on Ras by CDC25 and to accelerate Ras hydrolysis of GTP by p120GAP (3).

As an active metabolite of sulindac (a nonsteroidal anti-inflammatory drug or NSAID), sulindac sulfide inhibits growth and induces apoptosis in human prostate cancer cells through a COX-1- and COX-2independent mechanism (4,5). Growth inhibition appears to occur irrespective of androgen sensitivity or increased expression of bcl-2 (4). Sulindac sulfide has also been shown to up-regulate the prostate apoptosis response 4 (Par-4) gene in prostate carcinoma cells undergoing apoptosis (5).

Preparation Instructions

Soluble in DMSO (22 mg/ml).

Storage/Stability

Store tightly sealed at room temperature.

References

1. Rommel, C., et al., Science, **286**, 1738-1741, (1999).
2. Zimmermann, S. and Moelling, K. Science, **286**, 1741-1744, (1999).
3. Herrmann, C., et al., Oncogene **17**, 1769-1776, (1998).
4. Lim, J.T., et al., Biochem. Pharmacol. **58**, 1097-1107, (1999).
5. Zhang, Z. and DuBois, R.N. Gastroenterology, **118**, 1012-1017, (2000).

RB/MS 8/00