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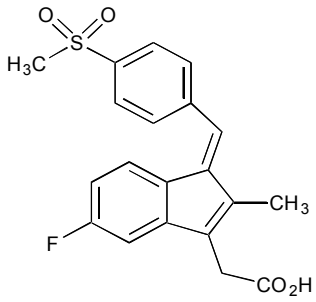
Product Information

Sulindac sulfone

Catalog Number **S1438**
Store at Room Temperature

CAS RN 59864-04-9
Synonym: (Z)-5-Fluoro-2-methyl-1-[p-(methylsulfonyl) benzylidene]indene-3-acetic acid



Product Description
Molecular Formula: C_{20} H_{17} FO_4 S
Formula Weight: 372.41
Supplied as yellow solid

Non-steroidal anti-inflammatory drugs (NSAIDs) suppress inflammation and pain by inhibiting the activity of cyclooxygenases (COX1 and COX2) and, thus, the production of prostaglandin E_2 and its metabolites. NSAIDs, such as sulindac, are also proapoptotic to many transformed cell lines and the chronic use of these agents has been associated with decreased mortality from colorectal cancer.[1]

Sulindac is metabolized *in vivo* to the sulfide and sulfone derivatives. Both derivatives have antineoplastic and proapoptotic properties. Although many tumor cells overexpress COX2, sulindac sulfone, unlike sulindac and sulindac sulfide, does not inhibit COX activity at physiological concentrations. However, sulindac sulfone does inhibit the expression of COX2 in Caco-2 human colon cancer cells that are transfected with the activated K-ras oncogene.[2]

Sulindac sulfone has been shown to induce apoptosis in more than 40 cancer cell lines. The mechanism of action appears to involve the inhibition of the type 5 cyclic GMP phosphodiesterases (PD5). This family of enzymes is overexpressed in colon, prostate, and lung cancer cell lines. Inhibition of PD5 increases intracellular cGMP which, in turn, activates protein kinase G (PKG). PKG phosphorylates (activates) mitogen-activated protein kinase kinase kinase (MEKK1) which, in turn, activates stress-activated protein kinase/ERK kinase 1 (SEK1), which then activates c-Jun NH_2-terminal kinase 1 (JNK1). The sustained activation of JNK1 leads to apoptosis through the activation of intracellular caspases.[3,4]

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
Sulindac sulfone is soluble in DMSO (25 mg/ml), in prewarmed ethanol (3 mg/ml), and in acetone (50 mg/ml).

Storage/Stability
Store the product at room temperature.

References
1. Rice, P.L., et al., Inhibition of extracellular signal-regulated kinase 1/2 phosphorylation and induction of apoptosis by sulindac metabolites. Cancer Res., **61**, 1541-1547 (2001).
2. Taylor, M.T., et al., Sulindac sulfone inhibits K-ras-dependent cyclooxygenase-2 expression in human colon cancer cells. Cancer Res., **60,** 6607-6610 (2000).
3. Myers, C., et al., Proapoptotic anti-inflammatory drugs**.** Urology, **57**, Suppl 1, 73-76 (2001).
4. Soh, J.W., et al., Cyclic GMP mediates apoptosis induced by sulindac derivatives via activation of c-Jun NH_2-terminal kinase1. Clin. Cancer Res., **10**, 4136-4141 (2000).

NRC,NC,KAA,LY,MAM 03/10-1