BW B70C

Product Number B 4558
Storage Temperature 2–8 °C

Cas Number:  134470-38-5
Synonyms: N-[3-[4-(Fluorophenoxy)phenyl]-1-methyl-2-propenyl]-N-hydroxyurea

Product Description
Molecular Formula: C_{17}H_{17}FN_{2}O_{3}
Molecular Weight: 316.32
Appearance: white solid
Purity: >98% by HPLC
Melting Point: 131-132.5 °C

The leukotrienes (LTs) comprise two classes of biologically active arachidonic acid derivatives. The hydroxyacid LTB_4 is a potent chemoattractant for neutrophils and functions as a proinflammatory mediator in immune response regulation. The cysteinyl leukotrienes, LTC_4, LTD_4 and LTE_4, are constrictors of vascular and airway smooth muscle that mediate inflammation in anaphylaxis, allergic rhinitis and asthma. 5-Lipoxygenase is the key enzyme in the biosynthetic pathway leading to the production of the leukotrienes. It catalyzes the oxidation of arachidonic acid to yield 5-hydroperoxy-6,8,11,14-eicosatetraenoic acid (5-HPETE). 5-HPETE is rapidly converted to the epoxide LTA_4. This unstable epoxide is metabolized to LTB_4 or LTC_4 by LTA_4 hydrolase or LTC_4 synthase, respectively.

There are three classes of 5-lipoxygenase inhibitors: iron chelating redox inhibitors, competitive reversible inhibitors (alternative substrates), and inhibitors of 5-lipoxygenase activating protein (FLAP). The most successful efforts to obtain potent and non-toxic inhibitors of 5-lipoxygenase have been in the synthesis of hydroxamic acid analogs and N-hydroxyurea derivatives whose functional groups chelate iron and, thus, inhibit the enzyme. The N-hydroxyurea derivative BW B70C is a potent iron chelating redox-type inhibitor of 5-lipoxygenase. At higher concentrations it also exhibits significant inhibition of cyclooxygenase and 15-lipoxygenase. BW B70C inhibits 5-lipoxygenase with an IC_{50} of approximately 0.2 µM and rabbit reticulocyte 15-lipoxygenase with an IC_{50} of approximately 30 µM. The dual action of BW B70C was shown in vivo in studies in guinea pigs comparing BW B70C with: the selective 5-lipoxygenase inhibitor ZD-2138. The animals were pretreated with BW B70C (50 mg/kg) or ZD-2138 prior to inhalation challenge with the allergen ovalbumin. Both compounds inhibited airway bronchoconstriction by blocking the 5-lipoxygenase pathway. In contrast, BW B70C but not ZD-2138, significantly inhibited mucus secretion. Since ZD-2138 is a potent, selective 5-lipoxygenase inhibitor that does not inhibit cyclooxygenase, 12-, or 15-lipoxygenase, the inhibition of mucus production by BW B70C was thought to be due to inhibition of the 15-lipoxygenase pathway.

BW B70C administered orally to allergen-sensitized guinea pigs inhibited bronchoconstriction and late-phase eosinophil accumulation induced by inhalation of allergen. Monocytes from allergic patients are hyperactivated. They produce high levels of LTB_4, express CD23, and demonstrate increased oxidative metabolism. BW B70C significantly suppresses monocyte hyperactivation.

5-Lipoxygenase inhibitors were used to study the involvement of lipoxygenase metabolites on tumor growth. BW A4C and BW B70C inhibited the growth of murine adenocarcinomas (MACs) in vitro with an IC_{50} < 10 µM.

Preparation Instructions
BW B70C is soluble in DMSO at 22 mg/ml.

Storage/Stability
BW B70C should be stored tightly sealed at 2-8 °C with desiccant.
References