Inhibitors, Agonists, Screening Libraries

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Data Sheet

Product Name: MK591
Cat. No.: HY-50714
CAS No.: 147030-01-1
Molecular Formula: C_{34}H_{34}ClN_{2}NaO_{3}S
Molecular Weight: 609.15
Target: FLAP
Pathway: Immunology/Inflammation
Solubility: 10 mM in DMSO

BIOLOGICAL ACTIVITY:
MK591 is a selective and specific 5–lipoxygenase–activating protein (FLAP) inhibitor.

In Vitro: MK591 and SB203580 are able to block SEB–induced human PBMC cell proliferation. MK591 down regulates three genes [for cathepsin L, IL–17 and guanylate binding protein (GBP)–2] that are up regulated by SEB\[1\]. MK591 undergoes apoptosis within hours of treatment. MK591 also induces rapid activation of the stress kinase, c–Jun N–terminal kinase (JNK), which plays an important role in the apoptosis process. MK591 triggers apoptosis in prostate cancer cells without inhibition of PI3K–Akt, or ERK.
Moreover, MK591 and LY294002 (an inhibitor of PI3K) exert synergistic effect in inducing apoptosis in prostate cancer cells\[2\]. MK–591 influences cAMP response element–binding protein but not Sp1\[4\].

In Vivo: Hyperoxia groups of mice treated with MK–0591 (20, 40 mg/kg) show alveolarization that resembles that of room air controls while untreated hyperoxia groups show definite evidence of aberrant alveolarization but no inflammation\[3\]. Comparison of the Aβ–immunopositive areas between the placebo and MK–591 (320 mg/kg)–treated group reveals a statistically significant reduction of the amyloid burden in the treated mice. MK–591 also has a significant reduction in brain levels of IL–1β. Mice treated with MK–591 show a statistically significant decrease in the steady–state levels of total CREB and its phosphorylated form at Ser133\[4\].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [2\]LNCaP cells (appr 3 \times 10^5) are plated and treated with inhibitors or solvent vehicle for varying periods of time. Then the cells are lysed in lysis buffer containing 0.2% CHAPS detergent plus protease and phosphatase inhibitors, and the enzymatic activity of Akt is measured by a kit following methods supplied by the manufacturer.

Animal Administration: [4]The Tg2576 transgenic mice expressing human APP with the Swedish mutation (K670N/M671L) are used in these studies. They are genotyped by PCR analysis using tail DNA and kept in a pathogen–free environment, on a 12–hour light/dark cycle and have access to food and water ad libitum. All the experiments presented in this paper are performed with female mice. Starting at 7 months of age, mice are randomized to receive MK–591 (40 mg/kg weight) (n=11) or vehicle (n=9) in their chow diet for 8 months until they are 15 months old. Considering that each mouse eats on average 5 g/day of chow diet and the diet is formulated for 320 mg MK–591 per kg diet, the final dose of the active drug is approximately 40 mg/kg weight/day. During the study, mice in both groups gain weight regularly, and no significant difference in weight is detected between the two groups. No macroscopic effect on the overall general health is observed in the animals receiving the active treatment. Post–mortem examination shows no sign of macroscopic pathology in any of the organs considered (spleen, liver, thymus, ileum).

References:
