FR194738

Cat. No.: HY-100303A
CAS No.: 204067-52-7
Molecular Formula: C₂₇H₃₈ClNO₂S
Molecular Weight: 476.11
Target: Others
Pathway: Others
Storage: Powder
-20°C 3 years
-4°C 2 years
In solvent
-80°C 6 months
-20°C 1 month

BIOLOGICAL ACTIVITY

Description
FR194738 is a squalene epoxidase inhibitor. FR194738 inhibits squalene epoxidase activity in HepG2 cell homogenates with an IC₅₀ of 9.8 nM.

IC₅₀ & Target
IC₅₀: 9.8 nM (squalene epoxidase, in HepG2 cell homogenates)[1]

In Vitro
In intact HepG2 cells, FR194738 concentration-dependently inhibits the incorporation of [¹⁴C]acetate into free cholesterol and cholesteryl ester, with IC₅₀s of 4.9 and 8.0 nM, respectively. FR194738 induces intracellular [¹⁴C]squalene accumulation. FR194738 increases the incorporation of [¹⁴C]acetate into squalene, an intermediate of cholesterol synthesis[1]. FR194738 potently inhibits squalene epoxidase (SE) in HepG2 cell homogenate and liver microsomes in dogs and rats. The inhibitory effect of FR194738 in comparison to the HMG-CoA reductase inhibitors, Simvastatin, Fluvastatin and Pravastatin, on cholesterol biosynthesis in HepG2 cells is examined. Among these compounds, FR194738 is the most potent, with an IC₅₀ of 2.1 nM. The IC₅₀s of Simvastatin, Fluvastatin and Pravastatin are 40, 28 and 5100 nM, respectively[2]. FR194738 inhibits hamster liver microsomal squalene epoxidase activity in a concentration-dependent manner with an IC₅₀ of 14 nM[3].

In Vivo
Serum lipid levels in hamsters after daily administration of FR194738 and Pravastatin for 10 d are measured. FR194738 reduces the serum levels of total, non high density lipoprotein (HDL) and HDL cholesterol, and triglyceride. Treatment of hamsters with FR194738 increases HMG-CoA reductase activity by 1.3-fold at 32 mg/kg compared to the control group and does not significantly change that at 100 mg/kg[3].

PROTOCOL

Cell Assay[1]
HepG2 cells are grown in 225 cm² culture flasks, and incubated for 18 h in medium A containing 10% human lipoprotein deficient serum and 1 μM L-654,969 to increase their squalene epoxidase activity. The HepG2 cells are washed and harvested by trypsin treatment. After centrifugation (1000×g, 5 min at 4°C), the supernatant fraction is removed by aspiration. The cell pellet is frozen and kept at -80 °C until use. On the day of the experiment, the stocked cell pellet is thawed, ruptured by sonication (5 s at 4°C) in 0.1 M Tris-HCl, pH 7.5 containing 1 mM EDTA, mixed with one-fourth volume of 2% Triton X-100, stood at 4°C for 30 min, and assayed for squalene epoxidase activity.
activity with some modifications. Aliquots of the mixture are incubated for 90 min at 37 °C with or without test compound (FR194738; 0.01 nM, 0.1 nM, 1 nM, 10 nM, 100 nM, 1 μM, and 10 μM) dissolved in DMSO (final 1%) in a final volume of 0.3 mL containing 0.1 M Tris-HCl, pH 7.5, 1 mM EDTA, 1 mM NADPH, 0.1 mM FAD, 0.3 mM AMO1618, an inhibitor of 2,3-oxidosqualene cyclase, 0.17% Triton X-100, and 8 μM [3H]squalene (3.7 kBq) dispersed in 0.075% Tween 80. The reaction is stopped by the addition of 0.3 mL of 10% ethanolic KOH. After incubation for 90 min at 75°C, non-saponifiable materials are extracted with 2 mL of petroleum ether. The extracts are evaporated under a nitrogen stream. The residue is taken up in a small volume of diethylether, spotted on a silica gel thin layer chromatography (TLC) plate and developed in benzene/ethyl acetate (99.5:0.5, v/v)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Animal Administration**[3]

**Six-week-old male golden Syrian hamsters (70-110 g)** are used. Drugs are administered as a diet mixture for 10 d. Blood samples are collected via heart puncture under ether anesthesia and serum is prepared by centrifugation. The dose of 0.32% in diet corresponds to 127 and 116 mg/kg/d for FR194738 and Pravastatin, respectively, calculated from body weight and food intake.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**


Caution: Product has not been fully validated for medical applications. For research use only.
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