# Data Sheet

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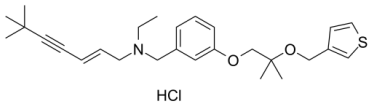
| **Product Name:** | FR194738 |
| **Cat. No.:** | CS-0006187 |
| **CAS No.:** | 204067-52-7 |
| **Molecular Formula:** | C27H38ClNO2S |
| **Molecular Weight:** | 476.11 |
| **Target:** | Others |
| **Pathway:** | Others |
| **Solubility:** | 10 mM in DMSO |




## BIOLOGICAL ACTIVITY:

FR194738 is a **squalene epoxidase** inhibitor. FR194738 inhibits squalene epoxidase activity in HepG2 cell homogenates with an $IC_{50}$ 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 [$^{14}$C]acetate into free cholesterol and cholesteryl ester, with $IC_{50}$s of 4.9 and 8.0 nM, respectively. FR194738 induces intracellular [$^{14}$C]squalene accumulation. FR194738 increases the incorporation of [$^{14}$C]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 $IC_{50}$ of 2.1 nM. The $IC_{50}$s 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 $IC_{50}$ 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 (Extracted from published papers and Only for reference)

**Cell Assay:** [1]**HepG2 cells** are grown in 225 $cm^2$ 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 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 [$^3$H]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].

**Animal Administration:** [3]Hamsters[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.

## References:

[1]. Sawada M, et al. Effect of FR194738, a potent inhibitor of squalene epoxidase, on cholesterol metabolism in HepG2 cells. Eur J Pharmacol. 2001 Nov 9;431(1):11-6.

[2]. Sawada M, et al. Synthesis and biological activity of a novel squalene epoxidase inhibitor, FR194738. Bioorg Med Chem Lett. 2004 Feb 9;14(3):633-7.

[3]. Sawada M, et al. Inhibition of cholesterol synthesis causes both hypercholesterolemia and hypocholesterolemia in hamsters. Biol Pharm Bull. 2002 Dec;25(12):1577-82.

## CAIndexNames:

Benzenemethanamine, N-[(2E)-6,6-dimethyl-2-hepten-4-yn-1-yl]-N-ethyl-3-[2-methyl-2-(3-thienylmethoxy)propoxy]-, hydrochloride (1:1)

## SMILES:

CC(OCC1=CSC=C1)(C)COC2=CC(CN(C/C=C/C#CC(C)(C)C)CC)=CC=C2.Cl



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