# Fenretinide

**Cat. No.:** HY-15373

**CAS No.:** 65646-68-6

**Molecular Formula:** $C_{26}H_{33}NO_2$

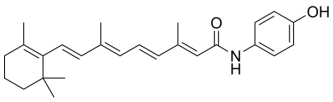
**Molecular Weight:** 392

**Target:** RAR/RXR; Autophagy

**Pathway:** Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor; Autophagy

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |




## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 130 mg/mL (331.63 mM)

* "≥" means soluble, but saturation unknown.

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.5510 mL | 12.7551 mL | 25.5102 mL |
| | 5 mM | 0.5102 mL | 2.5510 mL | 5.1020 mL |
| | 10 mM | 0.2551 mL | 1.2755 mL | 2.5510 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.38 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.38 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.38 mM); Clear solution

## BIOLOGICAL ACTIVITY

**Description**

Fenretinide (4-HPR) is a synthetic retinoid deriverative, binding to the retinoic acid receptors (RAR) at concentrations necessary to induce cell death.

**In Vitro**

Fenretinide (4-HPR) exerts not just acute but also long term antitumor activity in selected T-ALL cell lines. Fenretinide inhibits DES activity in CCRF-CEM leukemia cells in a dose and time dependent manner, leading to a concomitant increase of the endogenous cellular dhCer content. Fenretinide (3 μM)-induced dhCer accumulation in both CCRF-CEM and Jurkat cells

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| | [1]. Ceramide inhibition with fenretinide protects insulin signaling. Fenretinide prevents lipid-induced reductions in insulin-stimulated glucose uptake[2]. Fenretinide inhibits OVCAR-5 cell proliferation and viability at concentrations higher than 1 microM, with 70-90% growth inhibition at 10 microM. Fenretinide (1 microM) significantly inhibits OVCAR-5 invasion after 3 days preincubation. Endothelial cells treated with 1 microM 4-HPR fails to form tubes, but forms small cellular aggregates[4].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | Fenretinide (4-HPR) (10 mg/kg, i.p.) selectively inhibits ceramide accumulation HFD-fed male C57Bl/6 mice. Fenretinide treatment improves glucose tolerance and insulin sensitivity as determined by both glucose and insulin tolerance tests[2]. Addition of 25 mg/kg ketoconazole to Fenretinide in NOD/SCID mice increased 4-HPR plasma levels[3].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

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|---|---|
| **Cell Assay** [1] | Standard XTT assay is used to determine cell viability. For fenretinide-only treatments, cells are plated in 96-well plates at 750,000 cells/mL and 100 µL/well. After 4 h, treatments are added on 50 µL/well obtaining a final density of 500,000 cells/mL and final volume of 150 µL/well. Four replicates are used per experimental condition. XTT reagent mixture is added 4 h before the end of selected treatment period and absorbance at 490 nm is determined per each well. A slightly modified protocol is used for analysis of the effect of myriocin (final concentration of 100 nM) or antioxidant on Fenretinide treatment. Briefly, cells are seeded on 60 mm culture dishes and myriocin or antioxidants added after 4 h. Fenretinide treatment is added 2 h later and cells are plated in quadruplicates in 96 well plates (150 µL/well).<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [2] | Male mice (C57Bl6) are fed a standard chow or a high-fat diet (HFD) from 5 to 17 weeks, at which point half of the HFD-fed mice begin receiving fenretinide in drinking water for 4 weeks. Fenretinide is dissolved in 100% ethanol and diluted in water to 10 µg/mL. Control treatment water receives an equal amount of ethanol (0.5%). FEN water is prepared in low-light conditions and administered in light-protective bottles. Water is replaced every 1-2 days, and no precipitation of FEN is noted at any time. Animal weights are recorded at the beginning and end of the treatment period. Following a 4-week FEN treatment, mice undergo intraperitoneal glucose and insulin tolerance tests. For both tests, mice are fasted for 6 h andreceive an injection of either glucose (1 g/kg of body weight) or insulin (0.75 units/kg of body weight). Blood glucose is determined at the times indicated by the Bayer Contour® glucose meter, and insulin is measured with the rat/mouse insulin ELISA kit. The insulin resistance index is assessed by using fasting blood glucose and insulin levels to compute the homeostatic model assessment of insulin resistance (HOMA-IR), where a higher number represents greater insulin resistance.<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2022 Oct 24;7(1):370.
- Biomed Pharmacother. 2020 May;125:109680.
- Oncol Rep. 2018 Jul;40(1):518-526.
- J Cancer. 2019 Nov 1;10(27):6767-6778.
- Cornea. 2018 Dec;37(12):1579-1585.

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## REFERENCES

[1]. Apraiz, Aintzane., et al. Dihydroceramide accumulation and reactive oxygen species are distinct and nonessential events in 4-HPR-mediated leukemia cell death. Biochemistry and Cell Biology (2012), 90(2), 209-223.

[2]. Bikman, Benjamin T., et al. Fenretinide Prevents Lipid-induced Insulin Resistance by Blocking Ceramide Biosynthesis. Journal of Biological Chemistry (2012), 287(21), 17426-17437.

[3]. Cooper JP, et al. Fenretinide metabolism in humans and mice: utilizing pharmacological modulation of its metabolic pathway to increase systemic exposure. Br J Pharmacol. 2011 Jul;163(6):1263-75.

[4]. Golubkov V, et al. Action of fenretinide (4-HPR) on ovarian cancer and endothelial cells. Anticancer Res. 2005 Jan-Feb;25(1A):249-53.



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