Fulvestrant

Cat. No.: HY-13636

CAS No.: 129453-61-8

Molecular Formula: $C_{32}H_{47}F_5O_3S$

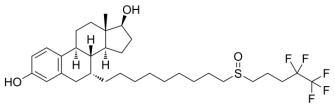
Molecular Weight: 606.77

Target: Estrogen Receptor/ERR; Autophagy; Apoptosis

Pathway: Vitamin D Related/Nuclear Receptor; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (412.02 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6481 mL	8.2404 mL	16.4807 mL
	5 mM	0.3296 mL	1.6481 mL	3.2961 mL
	10 mM	0.1648 mL	0.8240 mL	1.6481 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 2.75 mg/mL (4.53 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.12 mM); Suspended solution
3. Add each solvent one by one: 15% Solutol HS 15 >> 10% Cremophor EL >> 35% PEG 400 >> 40% water
   Solubility: 2.5 mg/mL (4.12 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.08 mg/mL (3.43 mM); Suspended solution; Need ultrasonic
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Fulvestrant (ICI 182780) is a pure antiestrogen and a potent estrogen receptor (ER) antagonist with an IC_{50} of 9.4 nM. Fulvestrant is also a GPR30 agonist. Fulvestrant effectively inhibits the growth of ER-positive MCF-7 cells with an IC_{50} of 0.29 nM. Fulvestrant also induces autophagy and has antitumor efficacy[1].

IC_{50} & Target	IC50: 9.4 nM (Estrogen Receptor)[1]
In Vitro	Fulvestrant (ICI 182780; ZD 9238; ZM 182780) is a potent and specific inhibitor of estrogen action and demonstrates excellent growth-inhibitory effects in both cell and animal models of human breast cancer. Fulvestrant inhibits MCF-7 human breast cancer cells growth with the IC_{50} of 0.29 nM. The relative binding affinities of Fulvestrant is 0.89. Fulvestrant has significantly increased antiestrogenic potency and retains pure estrogen antagonist activity[1]. Fulvestrant is the first of a new type of endocrine treatment-an oestrogen receptor (ER) antagonist that downregulates the ER[3]. Treatment of MCF-7 cells with 1 μM ICI 47699 has no effect on the expression of ERα, whereas 100 nM Fulvestrant completely inhibits ERα expression[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	When administered alone, parenterally (s.c.), Fulvestrant (ICI 182,780) is devoid of uterotropic activity in immature female rats. Fulvestrant (0.5 mg/kg/day s.c) shows complete antagonism of Estrogen action. Fulvestrant by po administration (5 mg/kg/day p.o.) is qualitatively similar with s.c.[1]. In two models of human breast cancer in nude mice. In one of these models, Fulvestrant (5 mg) completely blocks the growth of MCF-7 tumor xenografts for at least 4 weeks following a single injection. In other studies in nude mice bearing MCF-7 xenografts, Fulvestrant suppresses the growth of established tumours for twice as long and tumor growth is delayed to a greater extent than is observed with ICI 47699 treatment[3]. Fulvestrant exhibits tumor growth inhibition (TGI) on day 40 of 88%[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]	MCF-7 or T47D cells are cultured in 10 cm dishes to ~75% confluence in EMEM growth medium. Twenty-four hours before treatment, the growth medium is replaced with phenol red-free RPMI-1640 growth medium. A stock solution of 10 mM RAD1901 is prepared in DMSO. Dilutions of RAD1901 are prepared in RPMI growth medium (doses ranging from 10 to 0.5 nM). Controls include 0.1% DMSO alone (vehicle), 100 nM Fulvestrant, and 1 μM ICI 47699. Plated cells are treated with RAD1901 or controls for 48 h, and then incubated for 15 min with ice-cold lysis buffer [1 mM EDTA, 0.5% Triton X-100, 5 mM NaF, 6 M urea, 1 mM sodium orthovanadate, 2.5 mM sodium pyrophosphate, and 1× HALT protease inhibitor cocktail]. Lysates are centrifuged at 2000g for 5 min, and the supernatant is diluted 1 : 1 in lysis buffer. Ninety-six-well plates are coated overnight with capture antibody (1 μg/mL), washed three times in the manufacturer's wash buffer, blocked with blocking buffer for 2 h, and washed again. The prepared plates are incubated with 100 μL of the prepared cell lysate for 2 h, washed, incubated with biotinylated detection antibody for 2 h, and washed again. After a 20 min incubation with streptavidin-horseradish peroxidase, the plates are washed and incubated with substrate solution for 20 min. The reaction is stopped with stop solution, and the plates are analyzed on a microplate reader (OD_{450})[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][3]	Rats[1] In studies with OVX rats, surgical preparation is performed at least 2 weeks before treatment began. To measure the duration of action of a single large dose of Fulvestrant, OVX rats are treated with a daily s.c. dose of 0.5 μg of estradici benzoate beginning on the day of Fulvestrant administration and continued until vaginal smears showed evidence of cornification. At that point the experiment is terminated and uterine weight is recorded. The arachis oil formulation used in these single dose duration of action studies contained 50 mg Fulvestrant/mL. Mice[3] Female athymic nude mice [Crl:NU(NCr)-Foxn1nu] are used for tumor xenograft studies. Fourteen days after tumor cell implantation (designated as day 1 of the study), mice are 9 weeks of age, with body weights ranging from 21.4 to 32.5 g, individual tumor volumes ranging from 75 to 144 mm^3, and a group mean tumor volume (MTV) of 108 mm^3. The mice are randomized into nine groups of 15 animals each and treated with vehicle, ICI 47699 (1 mg/animal every other day), Fulvestrant (0.5 mg/animal daily), or RAD1901 (0.3, 1, 3, 10, 30, 60, 90, and 120 mg/kg daily). Tumor volumes are evaluated twice per week. The tumor endpoint is defined as an MTV of 1500 mm^3 in the control group. Animals are also monitored for partial regression (PR) and complete regression responses. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Cell. 2020 Mar 16;37(3):387-402.e7.
- Adv Sci (Weinh). 2023 Mar 11;e2300311.
- Nucleic Acids Res. 2020 Nov 4;48(19):10768-10784.
- Acta Pharm Sin B. 2021 Feb;11(2):442-455.
- J Med Virol. 2021 Jun;93(6):3769-3778.

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REFERENCES

[1]. Wakeling AE, et al. A potent specific pure antiestrogen with clinical potential. Cancer Res. 1991 Aug 1;51(15):3867-73.

[2]. Osborne CK, et al. Fulvestrant: an oestrogen receptor antagonist with a novel mechanism of action. Br J Cancer. 2004 Mar;90 Suppl 1:S2-6.

[3]. Garner F, et al. RAD1901: a novel, orally bioavailable selective estrogen receptor degrader that demonstrates antitumor activity in breast cancer xenograft models. Anticancer Drugs. 2015 Oct;26(9):948-56

[4]. Yu X, et al.MiR-214 increases the sensitivity of breast cancer cells to tamoxifen and fulvestrant through inhibition of autophagy.Mol Cancer. 2015 Dec 15;14:208.

[5]. Julia Kuhn, et al. GPR30 estrogen receptor agonists induce mechanical hyperalgesia in the rat. Eur J Neurosci. 2008 Apr;27(7):1700-9.

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