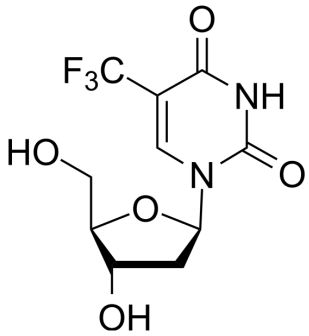
Trifluridine



Cat. No.:	HY-A0061
CAS No.:	70-00-8
Molecular Formula:	$C_{10}H_{11}F_3N_2O_5$
Molecular Weight:	296.2
Target:	Thymidylate Synthase; HSV; Nucleoside Antimetabolite/Analog; Orthopoxvirus; DNA/RNA Synthesis; Apoptosis; Autophagy
Pathway:	Apoptosis; Anti-infection; Cell Cycle/DNA Damage; 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 : ≥ 100 mg/mL (337.61 mM)

H_2O : 33.33 mg/mL (112.53 mM; ultrasonic and warming and heat to 60°C)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.3761 mL	16.8805 mL	33.7610 mL
5 mM	0.6752 mL	3.3761 mL	6.7522 mL
10 mM	0.3376 mL	1.6880 mL	3.3761 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 (8.44 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (8.44 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (8.44 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Trifluridine (Trifluorothymidine) is an irreversible and orally active thymidylate synthase inhibitor, and thereby suppressing DNA synthesis. Trifluridine is an antiviral molecule used for research of HSV, rhabdovirus and orthopoxvirus infection. Trifluridine induces cell apoptosis and autophagy. Trifluridine is also an anticancer agent used in studies of metastatic colorectal cancer, gastrointestinal tumors[1][2][3][4].

IC_{50} & Target	Thymidylate Synthase	Nucleoside Antimetabolite/Analog	HSV-1	HSV-2

In Vitro

Trifluridine (0.5 μM, 3 days) induces cellular senescence in HUVECs[2].
Trifluridine (0.5 μM, 3 days) inhibits autophagy and autophagy flux via the mTOR pathway in HUVECs [2].
Trifluridine (0-5 μM, 3 days) inhibits HUVEC cells viability in a concentration-dependent way[2].
Trifluridine (5 μM-20 μM, 24 h–72 h) inhibits the proliferation in MCF-7, MDA-MB-231, BT-549 and Hs578T[4].
Trifluridine (0 μM-20 μM, 48 h) selectively induces apoptosis in MCF-7, MDA-MB-231, BT-549 and Hs578T cells [4].
Trifluridine (10 μM, 72 h) induces DNA double-strand break in MCF-10A, MCF-7, MDA-MB-231 and BT-549 cells[4].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[2]

Cell Line:	HUVEC cells
Concentration:	0-5 μM
Incubation Time:	3 days
Result:	Cell viability dropped sharply at 3 μM and 5 μM.

Immunofluorescence[2]

Cell Line:	HUVEC cells
Concentration:	0-5 μM
Incubation Time:	3 days
Result:	Induced cellular senescence by inhibiting autophagy flux.

Western Blot Analysis[2]

Cell Line:	HUVEC cells
Concentration:	0-5 μM
Incubation Time:	3 days
Result:	Increased protein levels of senescence markers: p53, p16, SASP (IL-1, IL-6, TNF-α, p21).

Cell Proliferation Assay[4]

Cell Line:	MCF-7, MDA-MB-231, BT-549, Hs578T and MCF-10A(control non-tumor) cells
Concentration:	5 μM-20 μM
Incubation Time:	24 h–72 h
Result:	Inhibited the proliferation of MDA-MB231, BT549 and Hs578T cells at 10μM and 20μM, significantly.

Apoptosis Analysis[4]

Cell Line:	MDA-MB-231, BT-549, and Hs578T cells
Concentration:	10μM or 20 μM
Incubation Time:	48 h

Result:	Increased the percentages of apoptotic TNBC cells (MDA-MB-231, BT-549, and Hs578Tcells) at 10μM and 20μM, significantly.

In Vivo

Trifluridine/tipiracil (200 mg/kg, PO, twice daily for 5 consecutive days followed by 2 drug-free days for 6 weeks) shows antitumor activity in the human colorectal intraperitoneal xenograft model[3].
Trifluridine (75 or 150 mg/kg, oral gavage, once daily for 5 consecutive days) inhibits the growth in implanted mouse TNBC tumors [4].

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

Animal Model:	Nude mice (human colorectal intraperitoneal xenograft model)[3]
Dosage:	200 mg/kg(trifluridine/tipiracil)
Administration:	Oral administration; Once a day; 5 days followed by 2 drug-free days, a total of 6 weeks
Result:	Exhibited a significantly longer survival time compared with untreated mice.

Animal Model:	Mouse model of breast cancer[4]
Dosage:	75 or 150 mg/kg
Administration:	Oral gavage; daily for 10 days
Result:	Treatment with different doses inhibited the growth of TNBC tumors in mouse in a dose-dependent manner

Animal Model:	The human gastric MKN45 intraperitoneal xenograft model[3]
Dosage:	200 mg/kg (Trifluridine/tipiracil)
Administration:	twice daily for 5 consecutive days followed by 2 drug□free days for 6 weeks
Result:	Prolonged the survival of mice compared with untreated mice.

CUSTOMER VALIDATION

- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.

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REFERENCES

[1]. Jia HJ, et al. Trifluridine induces HUVECs senescence by inhibiting mTOR-dependent autophagy. Biochem Biophys Res Commun. 2022 Jun 25;610:119-126.

[2]. Suzuki N,et al. Trifluridine/tipiracil increases survival rates in peritoneal dissemination mouse models of human colorectal and gastric cancer. Oncol Lett. 2017 Jul;14(1):639-646.

[3]. Li J, et al. Trifluridine selectively inhibits cell growth and induces cell apoptosis of triple-negative breast cancer. Am J Cancer Res. 2020 Feb 1;10(2):507-522.

[4]. Okayama T, et al. Involvement of concentrative nucleoside transporter 1 in intestinal absorption of trifluorothymidine, a novel antitumor nucleoside, in rats. J

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