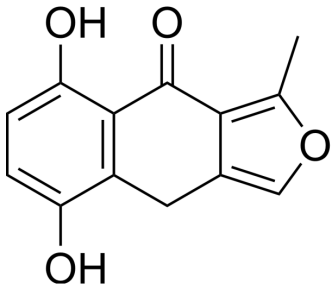
MS-444

Cat. No.:	HY-100685
CAS No.:	150045-18-4
Molecular Formula:	$C_{13}H_{10}O_4$
Molecular Weight:	230.22
Target:	Myosin
Pathway:	Cytoskeleton
Storage:	-20°C, protect from light, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (217.18 mM; Need ultrasonic)
1-Methyl-2-pyrrolidinone : 20 mg/mL (86.87 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	4.3437 mL	21.7184 mL	43.4367 mL
5 mM	0.8687 mL	4.3437 mL	8.6873 mL
10 mM	0.4344 mL	2.1718 mL	4.3437 mL

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

In Vivo

1. Add each solvent one by one: 10% 1-Methyl-2-pyrrolidinone >> 90% PBS
   Solubility: 2 mg/mL (8.69 mM); Suspended solution; Need ultrasonic and warming and heat to 50°C
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2 mg/mL (8.69 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2 mg/mL (8.69 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

MS-444 inhibits the activity of purified smooth muscle myosin light chain kinase (MLCK) with an IC_{50} value of 10 μM.

IC_{50} & Target

IC50: 10 μM (myosin)[1].

In Vitro

MS-444 is a small molecule RNA-binding protein HuR (ELAVL1) inhibitor. Colorectal cancer (CRC) cells that display HuR overexpression are treated with MS-444 (1-100 μM) for 48 hr with IC_{50}s of 10.98±1.76 μM, 12.84±2.10 μM, 5.60±0.90 μM, 14.21±2.11 μM, and 10.98±1.24 μM for HCT116, HCA-7, RKO, HT-29, and SW480 cells, respectively. Growth inhibition is

	observed in all CRC lines with IC_{50} values ranging from 5.60 μM to 14.21 μM with observable effects seen at 10 μM MS-444. Contrasting effects are observed using non-transformed small intestinal (RIE-1 (IC_{50}=40.70±3.53 μM)) and colonic (YAMC (IC_{50}=28.16±3.23 μM)) epithelial cells. Both cell types display properties of normal intestinal epithelial cells and are proficient in 3′UTR AU-rich elements (ARE)-mRNA decay. Both non-transformed cell lines are ~3- to 4-fold less responsive to MS-444-mediated growth inhibition, with IC_{50} values of 40.70 μM and 28.16 μM ($P<0.05$)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	To test the effects of MS-444 on CRC cell growth in vivo, mice bearing HCT116 cell xenografts receive IP injections of MS-444 (25 mg/kg bw) or vehicle every 48 hr. Over the experiment course, mice do not display any adverse effects and maintained similar weights. Anti-tumor effects of MS-444 are observed with approximately 1.7-fold reduction in tumor size. Mice treated with MS-444 show a marked 2- to 3-fold decrease in microvessel density (MVD), indicating the anti-angiogenic potential of MS-444[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Human colorectal cancer cell lines RKO, HCA-7, HCT116, HT-29, SW480 and the non-transformed intestinal epithelial cell lines RIE-1, YAMC are treated with varying concentrations of MS-444 (1-100 μM) for 48 hr. Cell survival is measured by MTT assay after incubation of cells for 48 hr with MS-444. Relative cell survival is calculated as percentage normalized to DMSO vehicle-treated cells and plotted to determine IC_{50}[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] Athymic nude (Nu/Nu) mice are used. HCT116 (2×10^6 cells) and HCA-7 (2.5×10^6) cells resuspended in PBS are injected into the dorsal subcutaneous tissue. Mice (n=5 per group) receive intraperitoneal (IP) injections of MS-444 (25 mg/kg) dissolved in PBS/5% N-Methyl Pyrrolidine (NMP) or vehicle control every 48 hr. Tumor growth is assayed[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- JCI Insight. 2023 Jan 5;e161961.

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REFERENCES

[1]. Satoshi Nakanishi. et al. MS-444, a new inhibitor of myosin light chain kinase from Micromonosporasp.KY7123. The Journal Of Antibiotics. 1995,48(9):948-951.

[2]. Fernando F. Blanco.et al, Impact of HuR inhibition by the small molecule MS-444 on colorectal cancer cell tumorigenesis. Oncotarget. 2016 Nov 8; 7(45): 74043-74058.

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