

Product Data Sheet

Product Name: MS-444 (BE-34776)

Cat. No.: GC33214

Chemical Properties

Cas. No. 150045-18-4

SMILES O=C(C1=C(C)OC=C1C2)C3=C2C(O)=CC=C3O

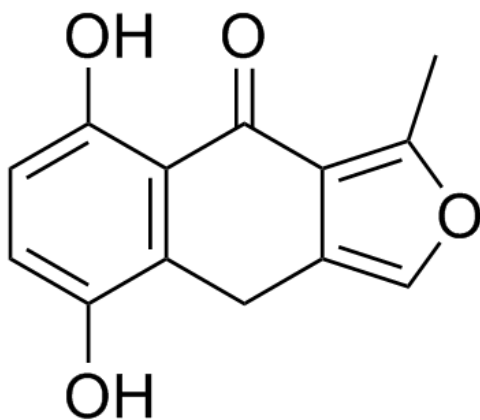
Formula $C_{13}H_{10}O_4$ M.Wt 230.22

Solubility DMSO: 12.5 mg/mL (54.30 mM) Storage Store at -20°C, protect from light, stored under nitrogen

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Cell experiment: 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 μ M) 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 IC₅₀[2].

Animal experiment: 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].

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.

Background

MS-444 inhibits the activity of purified smooth muscle myosin light chain kinase (MLCK) with an IC₅₀ value of 10 μ M.

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 μ M) for 48 hr with IC₅₀s of 10.98 ± 1.76 μ M, 12.84 ± 2.10 μ M, 5.60 ± 0.90 μ M, 14.21 ± 2.11 μ M, and 10.98 ± 1.24 μ M for HCT116, HCA-7, RKO, HT-29, and SW480 cells, respectively. Growth inhibition is observed in all CRC lines with IC₅₀ values ranging from 5.60 μ M to 14.21 μ M with observable effects seen at 10 μ M MS-444. Contrasting effects are observed using non-transformed small intestinal (RIE-1 (IC₅₀= 40.70 ± 3.53 μ M)) and colonic (YAMC (IC₅₀= 28.16 ± 3.23 μ M)) epithelial cells. Both cell types display properties of

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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 IC₅₀ values of 40.70 μ M and 28.16 μ M ($P < 0.05$)[2].

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].

[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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