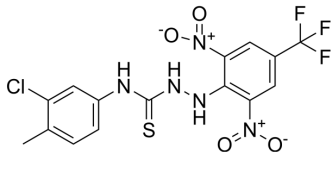
Kobe0065

Cat. No.:	HY-15716
CAS No.:	436133-68-5
Molecular Formula:	$C_{15}H_{11}ClF_3N_5O_4S$
Molecular Weight:	449.79
Target:	Ras; Apoptosis
Pathway:	GPCR/G Protein; Apoptosis
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 : ≥ 42.5 mg/mL (94.49 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2233 mL	11.1163 mL	22.2326 mL
5 mM	0.4447 mL	2.2233 mL	4.4465 mL
10 mM	0.2223 mL	1.1116 mL	2.2233 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 (5.56 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Kobe0065 is a novel and effective inhibitor of Ras-Raf interaction, competitively inhibiting the binding of H-Ras·GTP to c-Raf-1 RBD with a K_i value of 46±13 μM.

IC_{50} & Target

H-Ras

In Vitro

Kobe0065-family compounds bind to Ras•GTP and exhibit antiproliferative activity toward cancer cells carrying the activated ras oncogenes. The compounds efficiently inhibit the interaction of Ras•GTP with their multiple effectors including Raf, PI3K, and RalGDS and a regulator/effector Sos and show rather broad binding specificity toward various Ras family small GTPases, which may account for their higher potency at the cellular level compared with that of the in vitro binding inhibition[1]. The phosphorylation of downstream kinases MEK and ERK is effectively attenuated by 20 μM Kobe0065 and Kobe2602 in NIH3T3 cells transiently expressing H-RasG12V[2].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Kobe0065 and Kobe2602 exhibit antitumor activity on a xenograft of human colon carcinoma SW480 cells carrying the K-ras(G12V) gene by oral administration[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells (2×10^3) are seeded in a 96-well plate and cultured in DMEM containing 2% (vol/vol) FBS in the presence of one of the compounds. Viable cell numbers are measured by formazan formation using a Cell Counting Kit 8. Apoptotic cells are detected by a standard TUNEL assay using an In Situ Cell Detection kit. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Cells (5×10^6) are implanted into the right flanks of female athymic nude mice (6-8 wk old). After tumor sizes reached appr 50 mm^3 on average, compounds suspended in Cremophor:ethanol:water (1:1:6) are administered orally for five consecutive days per week for 17 d. Tumor volumes (V) are calculated. Dissected tumors after 17-d administration of the 80 mg/kg compounds are fixed in 4% (wt/vol) paraformaldehyde and embedded in paraffin. Their sections are subjected to immunohistochemistry with an anti-ERK1/2 antibody or an anti-CD31 antibody using a HISTMOUSE-PLUS kit. Apoptotic cells are detected by a TUNEL assay. Statistical significance for groups of three or more is determined by one-way ANOVA with Tukey's test for post hoc analysis. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- BMC Biol. 2022 Dec 13;20(1):278.
- Cell Signal. 2016 Feb;28(2):81-93.
- Respir Physiol Neurobiol. 2020 Oct;281:103496.

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REFERENCES

[1]. Shima, Fumi, et al. In silico discovery of small-molecule Ras inhibitors that display antitumor activity by blocking the Ras-effector interaction. Proceedings of the National Academy of Sciences of the United States of America (2013), 110(20), 8182-8187,

[2]. Shima F, et al. Discovery of small-molecule Ras inhibitors that display antitumor activity by interfering with Ras·GTP-effector interaction. Enzymes. 2013;34 Pt. B:1-23

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