MA242 free base

Cat. No.: HY-112816A

CAS No.: 1049704-17-7

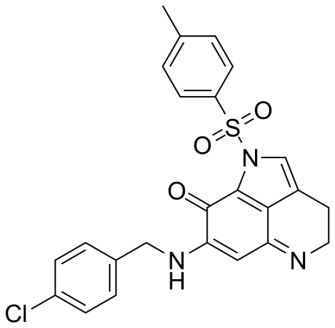
Molecular Formula: $C_{24}H_{20}ClN_3O_3S$

Molecular Weight: 465.95

Target: MDM-2/p53; Apoptosis

Pathway: Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

MA242 free base is a specific dual inhibitor of MDM2 and NFAT1. MA242 free base directly binds both MDM2 and NFAT1 with high affinity, induces their protein degradation, and inhibits NFAT1-mediated transcription of MDM2. MA242 free base induces apoptosis in pancreatic cancer cell lines regardless of p53 status[1].

IC_{50} & Target

MDM2, NFAT1[1]

In Vitro

MA242 (0.05-5 μM; 72 hours) free base significantly inhibits pancreatic cancer cell growth, with IC_{50}s ranging from 0.1 to 0.4 μM, regardless of the p53 status of the cells. However, MA242 free base shows minimal effects on the growth of normal HPDE cells (IC_{50}=5.81 μM), indicating that MA242 has selective effects against cancer cells[1].

MA242 (0.1-0.5 μM; 24 hours) free base significantly decreases the MDM2 and NFAT1 protein levels at a low concentration in all three cell lines[1].

MA242 free base decreases cell proliferation and induces apoptosis in pancreatic cancer cell lines regardless of p53 status[1].

MA242 free base alone or in combination with Gemcitabine inhibits pancreatic tumor growth and metastasis without any host toxicity[1].

MA242 free base exerts cytotoxicity against hepatocellular carcinoma (HCC) cells by inhibiting the NFAT1-MDM2 pathway in vitro, independent of p53. MA242 showed selective cytotoxicity against HCC cells, with IC_{50} values ranging from 0.1-0.31 μM [2].

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

Cell Viability Assay[1]

Cell Line:	The human pancreatic cancer HPAC, Panc-1, AsPC-1, Mia-Paca-2 and BxPC-3 cell lines; The human pancreatic ductal epithelium (HPDE) cell line
Concentration:	0.05, 0.5, and 5 μM
Incubation Time:	72 hours
Result:	The IC_{50}s are 0.14, 0.14, 0.15, 0.25, 0.40, and 5.81 μM for Panc-1, Mia-Paca-2, AsPC-1, BxPC-3, HPAC, and HPDE cells, respectively.

Western Blot Analysis[1]

Cell Line:	The human pancreatic cancer HPAC, Panc-1, and AsPC-1 cell lines

Concentration:	0, 0.1, 0.2, and 0.5 μM
Incubation Time:	24 hours
Result:	Decreased the expression of MDM2 and NFAT1.

In Vivo

MA242 (IP; 2.5, 5, 10 mg/kg) free base suppresses orthotopic pancreatic tumor growth in vivo, independent of p53[1].
There were no significant differences in the average body weights between the vehicle- and MA242 free base-treated mice in either of the models, did not have significant host toxicity at these effective doses[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Female 4-6-week-old athymic nude mice (nu/nu, 4-6 weeks) bearing AsPC-1-Luc or Panc-1-Luc tumor[1]
Dosage:	2.5 or 5 mg/kg for Panc-1 tumor-bearing mice; 10 mg/kg for AsPC-1 tumor-bearing mice
Administration:	IP; 2.5 or 5 mg/kg/d, 5 d/wk for five weeks for Panc-1 tumor-bearing mice; IP; 10 mg/kg/d, 5 d/wk for three weeks for AsPC-1 tumor-bearing mice
Result:	Resulted in 56.1% and 82.5% inhibition of tumor growth in nude mice bearing Panc-1 orthotopic tumors, respectively. Significantly suppressed the growth of AsPC-1 orthotopic tumors by 89.5% ($P < 0.01$) compared with the tumors in control animals. Led to almost complete tumor regression in MD242-treated mice in both models.

CUSTOMER VALIDATION

- Biochem Pharmacol. 2020 Apr;174:113795.

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REFERENCES

[1]. Wei Wang, et al. Discovery and Characterization of Dual Inhibitors of MDM2 and NFAT1 for Pancreatic Cancer Therapy. Cancer Res. 2018 Oct 1;78(19):5656-5667.

[2]. Wei Wang, et al. MDM2-NFAT1 dual inhibitor, MA242: Effective against hepatocellular carcinoma, independent of p53. Cancer Lett. 2019 Sep 10;459:156-167.

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