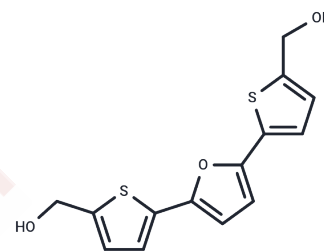


RITA

Chemical Properties

CAS No. : 213261-59-7
 Formula: C₁₄H₁₂O₃S₂
 Molecular Weight: 292.37
 Appearance: no data available
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year



Biological Description

Description	RITA (NSC-652287)(NSC-652287) induced cross-links of both DNA-DNA and DNA-protein with no detectable DNA single-strand breaks. RITA, like nutlin-3, can disrupt the p53/Mdm2 interaction.
Targets(IC ₅₀)	Mdm2, Autophagy, DNA Alkylator/Crosslinker, p53
In vitro	RITA (10 nM) caused cell cycle arrest and accumulation of cells in the G ₂ -M phase, and at 100 nM it induced DNA fragmentation and apoptosis and increased p53 protein levels. RITA (30 nM) also induced the production of DNA-protein and DNA-DNA crosslinks in A498 cells. At the same time, RITA did not affect top1-regulated superhelical SV40 DNA loosening. RITA significantly inhibited HCT116 cell growth (97%) and slightly inhibited HCT116 TP53-/- cell growth (13%). RITA inhibited the growth of wild-type p53-expressing cells more effectively than that of cells lacking p53 or with p53 mutation. When acting on tumor cells, RITA showed a high degree of selectivity for different toxicities due to the accumulation of cytoplasmic (S100) fractions. RITA bound to full-length p53 but not to glutathione S-transferase proteins or HDM-2. RITA also inhibited the growth of other renal cell lines including ACHN and UO-31 (IC ₅₀ : 13 μM and 37 μM). RITA blocked p53-HDM-2 interaction and p53 ubiquitination. RITA caused a significant decrease in the amount of HDM-2 co-precipitated with p53, although both proteins were up-regulated. RITA blocked the interaction between 6XHis-tagged His-HDM-2 protein and purified GST-p53. By promoting p53Ser46 phosphorylation, RITA induces apoptosis. RITA induced p53 activation and showed upregulation of phosphorylated MKK-4, ASK-1 and c-Jun. It also induced JNK signaling activation. NMR results showed that RITA did not block the formation of the complex between the N-terminal p53-binding domain (residues 1-118) and p53 (residues 1-312) of MDM2, which may be related to the fact that the binding of RITA requires the natural conformation of p53.
In vivo	RITA (10 nM) caused cell cycle arrest and accumulation of cells in the G ₂ -M phase, and at 100 nM it induced DNA fragmentation and apoptosis and increased p53 protein levels. RITA (30 nM) also induced the production of DNA-protein and DNA-DNA crosslinks in A498 cells. At the same time, RITA did not affect top1-regulated superhelical SV40 DNA loosening. RITA significantly inhibited HCT116 cell growth (97%) and slightly inhibited HCT116 TP53-/- cell growth (13%). RITA inhibited the growth of wild-type p53-expressing cells more effectively than that of cells lacking p53 or with p53 mutation. When acting on tumor cells, RITA showed a high degree of selectivity for different toxicities due to the accumulation of cytoplasmic (S100) fractions. RITA bound

to full-length p53 but not to glutathione S-transferase proteins or HDM-2. RITA also inhibited the growth of other renal cell lines including ACHN and UO-31 (IC₅₀: 13 μ M and 37 μ M). RITA blocked p53-HDM-2 interaction and p53 ubiquitination. RITA caused a significant decrease in the amount of HDM-2 co-precipitated with p53, although both proteins were up-regulated. RITA blocked the interaction between 6XHis-tagged His-HDM-2 protein and purified GST-p53. By promoting p53Ser46 phosphorylation, RITA induces apoptosis. RITA induced p53 activation and showed upregulation of phosphorylated MKK-4, ASK-1 and c-Jun. It also induced JNK signaling activation. NMR results showed that RITA did not block the formation of the complex between the N-terminal p53-binding domain (residues 1-118) and p53 (residues 1-312) of MDM2, which may be related to the fact that the binding of RITA requires the natural conformation of p53.

Kinase Assay	The inhibition profile of cabozantinib against a broad panel of 270 human kinases is determined using luciferase-coupled chemiluminescence, ³² P-phosphoryl transfer, or AlphaScreen technology. Recombinant human full-length, glutathione S-transferase tag, or histidine tag fusion proteins are used, and half maximal inhibitory concentration (IC ₅₀) values are determined by measuring phosphorylation of peptide substrate poly (Glu, Tyr) at ATP concentrations at or below the K _m for each respective kinase. The mechanism of kinase inhibition is evaluated using the AlphaScreen Assay by determining the IC ₅₀ values over a range of ATP concentrations.
Cell Research	Examination to assess susceptibility of cells to RITA (0.1 nM - 1 mM) is done using the XTT assay. Cells are inoculated into 96-well flat-bottom plates at a density of 1500 cells per well and incubated for 24 hours at 37 °C in a humidified 5% CO ₂ 5% air atmosphere. Serial concentrations of RITA in DMSO are added to the wells, and sensitivity is determined 48 hours after the addition of RIT (Only for Reference)

Solubility Information

Solubility	DMSO: 45 mg/mL (153.91 mM), Sonication is recommended. Ethanol: 7.3 mg/mL (24.97 mM), Sonication is recommended. (< 1 mg/mL refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.4203 mL	17.1016 mL	34.2032 mL
5 mM	0.6841 mL	3.4203 mL	6.8406 mL
10 mM	0.342 mL	1.7102 mL	3.4203 mL
50 mM	0.0684 mL	0.342 mL	0.6841 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

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