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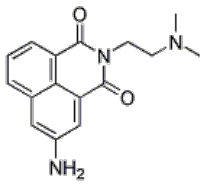
Amonafide Datasheet

Technical Data

Molecular Weight (MW)	283.33
Formula	$C_{16}H_{17}N_3O_2$
CAS No.	69408-81-7, 150091-68-2 (2HCl), 135882-21-2 (methanesulfonate)
Synonyms	AS1413, Xanafide, Quinamed

Solubility (25°C)	DMSO 57 mg/mL		
	Water <1 mg/mL		
	Ethanol 4 mg/mL		
Storage	2 years	-20°C	Powder
	2 weeks	4°C	in DMSO
	6 months	-80°C	in DMSO

Amonafide Chemical Structure



Biological Activity

Description	Amonafide (NSC-308847) is a selective **topoisomerase II** inhibitor.
Targets	Topoisomerase II
IC50	
In vitro	Through a topoisomerase II-mediated reaction, Amonafide treatment produces DNA single-strand breaks (SSB), double-strand breaks (DSB), and DNA-protein cross-links in human myeloid leukemia cells. Amonafide treatment inhibits conlony formation of the leukemic cell lines and the normal human bone marrow GM-CFC in a dose-dependent manner. Amonafide does not produce topoisomerase I-mediated DNA cleavage even at 100 μM. The m-AMSA-resistant line is less than 2-fold resistant to Amonafide [1] Amonafide interferes with the DNA breakage-reunion activity of mammalian DNA topoisomerase II resulting in DNA cleavage stimulation. [2] Compared with those of other antitumor drugs, Amonafide-stimulated cleavage intensity patterns are markedly different. Amonafide highly prefers a cytosine, and excludes guanines and thymines instead, at position -1, with lower preference for an adenine at position +1. [3] Topoisomerase II-mediated DNA cleavage induced by Amonafide is affected only slightly (less than 3-fold) by 1 mM ATP, suggeting that Amonafide is an ATP-insensitive topoisomerase II inhibitor in contrast to doxorubicin, etoposide, and mitoxantrone. [4] Amonafide significantly inhibits the growth of HT-29, HeLa, and PC3 cells with IC50 of 4.67 μM, 2.73 μM, and 6.38 μM, respectively. [5] Amonafide is unaffected by P-glycoprotein-mediated efflux, unlike those of the classical topoisomerase II inhibitors (daunorubicin, doxorubicin, idarubicin, etoposide, and mitoxantrone). [6]
In vivo	
Clinical Trials	A Phase I/II study of Amonafide in men with androgen-independent prostate cancer has been completed.
Features	

Protocol (Only for Reference)

Cell Assay: [5]

Cell Lines	HT-29, HeLa, and PC3
Concentrations	Dissolved in DMSO, final concentrations ~10 μM
Incubation Time	72 hours
Methods	All cell lines are in the logarithmic phase of growth when the assay of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) is carried out. Cells are harvested and seeded into 96-well tissue culture plates at a density of 2.5×10^3 cells/well in 150 μL aliquots of medium. The concentrations tested are serial dilutions of a stock solution (10 μM in DMSO) with phosphate-buffered saline (PBS) and are added 24 hours later. The assay is ended after 72 hours of Amonafide exposure and PBS is used as a negative control. After 72 hours treatment, cells are washed twice with PBS, and then 50 μL/well of MTT reagent (1 mg/mL in PBS) together with 150 μL/well of prewarmed medium are added. The plates are returned to the incubator for 4 hours. Subsequently, DMSO is added as solvent. Absorbance is determined at 570 nm with a Microplate reader. All experiments were performed at least three times, and the average of the percentage absorbance is plotted against concentration. Then, the concentration of Amonafide required to inhibit 50% of cell growth (IC50) is calculated for Amonafide.

References

[1] Andersson BS, et al. Cancer Res, 1987, 47(4), 1040-1044.
[2] Hsiang YH, et al. Mol Pharmacol, 1989, 36(3), 371-376.
[3] De Isabella P, Nucleic Acids Res, 1995, 23(2), 223-229.
[4] Wang H, et al. J Biol Chem, 2001, 276(19), 15990-15995.
[5] Braña MF, et al. J Med Chem, 2004, 47(6), 1391-1399.
[6] Chau M, et al. Leuk Res, 2008, 32(3), 465-473.

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