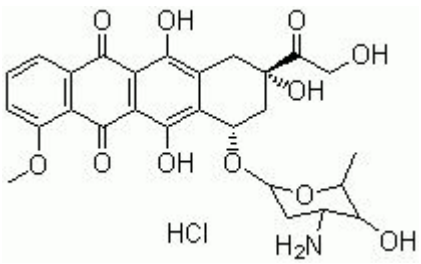
Biochempartner
瀚香生物科技

Product Introduction

Doxorubicin (Adriamycin)

Doxorubicin (Adriamycin) is an antibiotic agent that inhibits **DNA topoisomerase II** and induces DNA damage and apoptosis.

Technical Data:

Molecular Weight (MW):	579.98	
Formula:	$C_{27}H_{29}NO_{11}.HCl$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 100 mg/mL	
	Water 20 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	25316-40-9	

Biological Activity

Doxorubicin, an antibiotic anthracycline, is commonly considered to exert its anti-tumor activity at two fundamental levels, altering DNA and producing free radicals to trigger apoptosis of cancer cells through DNA damage. Doxorubicin can block the synthesis of DNA by intercalating into the DNA strand, and inhibits DNA topoisomerase II (TOP2). Doxorubicin is most effective when cells are rapidly proliferating and expressing high levels of TOP2. Additionally, Doxorubicin can trigger apoptosis by producing ceramide (which prompts apoptosis by activating p53 or other downstream pathways such as JNK), the degradation

of Akt by serine threonine proteases, the mitochondrial release of cytochrome c, increased FasL (death receptor Fas/CD95 ligand) mRNA production, and a greater production of free radicals. [2] Pre-treatment with GSNO (nitrosoglutathione) suppresses the resistance in the doxorubicin-resistant breast cancer cell line MCF7/Dx, accompanied by enhanced protein glutathionylation and accumulation of doxorubicin in the nucleus. [3] Doxorubicin induced G2/M checkpoint arrest are attributed to elevated cyclin G2 (CycG2) expression and phospho-modification of proteins in the ataxia telangiectasia mutated (ATM) and ATM and Rad3-related (ATR) signaling pathways. [5] Doxorubicin inhibits AMP-activated protein kinase (AMPK), resulting in SIRT1 dysfunction, p53 accumulation, and increased cell death in mouse embryonic fibroblasts (MEFs) and cardiomyocytes, which can be further sensitized by pre-inhibition of AMPK. [6] Doxorubicin elicits a marked heat shock response, and that either inhibition or silencing of heat shock proteins enhance the Doxorubicin apoptotic effect in neuroblastoma cells. Nanomolar Doxorubicin treatment of neuroblastoma cells causes dose-dependent over-ubiquitination of a specific set of proteins in the absence of measurable inhibition of proteasome, and loss of activity of ubiquitinated enzymes such as lactate dehydrogenase and α-enolase, the protein ubiquination patterns of which is similar to those with proteasome inhibitor Bortezomib, indicating that Doxorubicin may also exert its effect by damaging proteins. [8]

Doxorubicin in combination with adenoviral MnSOD (AdMnSOD) plus 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) has the greatest effect in decreasing the volumes of MB231 tumors and prolonging survival of mice. [1] Although its use is limited by the chronic and acute toxic side effects it produces, Doxorubicin is essential in treating breast and oesophageal carcinomas, solid tumours in childhood, osteosarcomas, Kaposi's sarcoma, soft tissue sarcomas, and Hodgkin and non-Hodgkin lymphomas. [2]

References

[1] Sun W, et al. Cancer Res, 2009, 69(10), 4294-4300.

[2] Granados-Principal S, et al. Food Chem Toxicol, 2010, 48(6), 1425-1438.

[3] de Luca A, et al. Biochem J, 2011, 440(2), 175-183.

[4] Cheriyath V, et al. Br J Cancer, 2011, 104(6), 957-967.

[5] Zimmermann M, et al. J Biol Chem, 2012, 287(27), 22838-22853.

[6] Wang S, et al. J Biol Chem, 2012, 287(11), 8001-8012.

[7] Luke JJ, et al. Clin Cancer Res, 2012, 18(9), 2638-2647.

[8] Mandili G, et al. FEBS J, 2012, 279(12), 2182-2191.