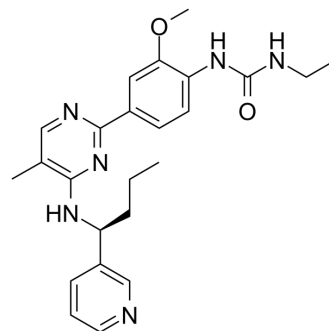


Lexibulin

Cat. No.:	HY-10498
CAS No.:	917111-44-5
Molecular Formula:	C ₂₄ H ₃₀ N ₆ O ₂
Molecular Weight:	434.53
Target:	Microtubule/Tubulin; Apoptosis; Reactive Oxygen Species
Pathway:	Cell Cycle/DNA Damage; Cytoskeleton; Apoptosis; Immunology/Inflammation; Metabolic Enzyme/Protease; NF-κB
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 : ≥ 100 mg/mL (230.13 mM) * "≥" means soluble, but saturation unknown.				
	Preparing Stock Solutions	<div>Solvent Concentration</div> <div>Mass</div>	1 mg	5 mg	10 mg
		1 mM	2.3013 mL	11.5067 mL	23.0134 mL
		5 mM	0.4603 mL	2.3013 mL	4.6027 mL
		10 mM	0.2301 mL	1.1507 mL	2.3013 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 (5.75 mM); Clear solution				
	2. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (5.75 mM); Clear solution				

BIOLOGICAL ACTIVITY

Description	Lexibulin (CYT-997) is a potent and orally active tubulin polymerisation inhibitor with IC50s of 10-100 nM in cancer cell lines; with potent cytotoxic and vascular disrupting activity in vitro and in vivo ^{[1][2]} . Lexibulin induces cell apoptosis and induces mitochondrial ROS generation in GC cells ^[3] .
IC ₅₀ & Target	IC50 value: 10-100 nM(cell assay) ^[1]
In Vitro	Lexibulin (CYT-997) prevents the in vitro polymerization of tubulin with an IC50 of 3 μmol/L (compared with the half-maximal inhibitory concentration of 2 μmol/L for colchicine under identical conditions) as determined using the

conventional turbidimetric assay for tubulin polymerization. Lexibulin is also capable of reversibly disrupting the microtubule network in cells, visualized using fluorescence microscopy. Thus, treatment of A549 cells with Lexibulin (1 μ M) lead to the rapid reorganization of microtubules, including the destruction of the existing microtubule network and accumulation of tubulin in plaques within the cytoplasm of some cells. After 24 hours, major alterations in cell morphology are evident, including loss of adhesion and cell rounding. The effect of 1 hour of treatment with Lexibulin is reversible and cells rapidly recovered their normal microtubule architecture. Taken together, the data indicates that Lexibulin belongs to the class of anticancer agents that disrupt, rather than stabilize, tubulin-containing structures. Although vehicle-treated cells show 15% and 19% in G2-M phase at 15 and 24 hours (respectively), cells treated with Lexibulin (1 μ M) had 38% and 43% of cells in G2-M at the same time points. Furthermore, at 24 hours post-Lexibulin treatment, only 66% of total cells are in the G1, S, and G2-M phases, which suggests that cells blocked at the G2-M boundary do not exit back to G1, as in the normal cell cycle, but most likely are driven towards apoptosis and cell death^[1]. Consistent with the disruption of cellular tubulin, Lexibulin potently inhibits proliferation, induces cell cycle arrest and most importantly apoptosis of both human myeloma cell lines (HMCLs) and primary MM cells^[2].

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

In Vivo

in a xenograft model using the human prostate cancer cell line PC3, oral dosing of Lexibulin (CYT-997) is initiated 13 days after cell implantation by which time palpable tumors were evident. A dose-dependent inhibition of tumor growth was apparent with Lexibulin (CYT-997), which at the highest dose was equivalent to parenterally administered paclitaxel. A single dose of Lexibulin (CYT-997) (7.5 mg/kg i.p.) clearly decreased blood flow in liver metastases, and a significant reduction in blood flow was present 6 hours postdose^[1]. Lexibulin (CYT-997) treatment (15 mg/kg/day) significantly prolongs the survival in a murine model of aggressive systemic myelomatosis^[2].

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

CUSTOMER VALIDATION

- J Exp Clin Cancer Res. 2020 Jun 23;39(1):119.

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REFERENCES

[1]. Burns CJ, et al. CYT997: a novel orally active tubulin polymerization inhibitor with potent cytotoxic and vascular disrupting activity in vitro and in vivo. Mol Cancer Ther. 2009 Nov;8(11):3036-45.

[2]. Monaghan K, et al. CYT997 causes apoptosis in human multiple myeloma. Invest New Drugs. 2011 Apr;29(2):232-8.

[3]. Ya Cao, et al. Mitochondrial ROS Accumulation Inhibiting JAK2/STAT3 Pathway Is a Critical Modulator of CYT997-induced Autophagy and Apoptosis in Gastric Cancer. J Exp Clin Cancer Res. 2020 Jun 23;39(1):119.

Caution: Product has not been fully validated for medical applications. For research use only.

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