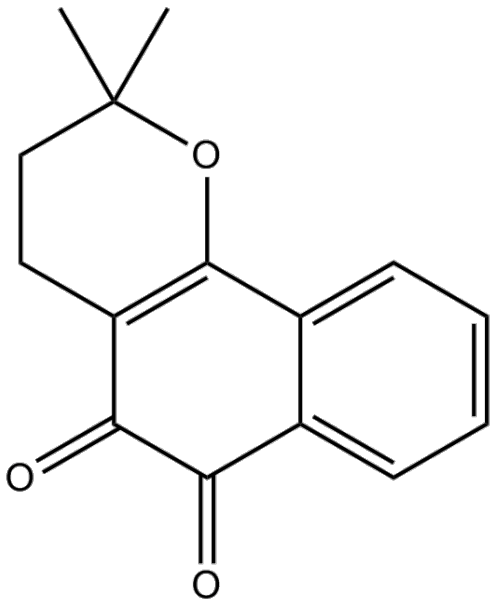
Product Data Sheet

Product Name: β-Lapachone
Cat. No.: GC10734

Chemical Properties

Cas. No.	4707-32-8		
Chemical Name	2,2-dimethyl-3,4-dihydrobenzo[h]chromene-5,6-dione		
SMILES	CC1(CCC2=C(O1)C3=CC=CC=C3C(=O)C2=O)C		
Formula	$C_{15}H_{14}O_3$	M.Wt	242.27
Solubility	≥ 10.85mg/mL in DMSO	Storage	Store at -20° C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	SW480 cells, SW620 cells, DLD1 cells
Preparation Method	Cells were seeded into 60mm dishes at a density of 7×10^{5} per dish. Colon cancer cells, SW480, SW620, and DLD1 cells, were transiently exposed to β-Lapachone (2.5 or 5μM) for 4h, further incubated in drug-free medium for 20h, and then analyzed for cell cycle distribution by flow-cytometric analysis. Cells were then harvested by trypsinization, and incubated for 30min at room temperature in staining solution consisting of propidium iodide (50μg/ml), sodium citrate (0.1%), Triton X-100 (0.1%), and DNase-free RNase (20μg/ml). Stained cells were then analyzed for DNA content by flow cytometry.
Reaction Conditions	2.5 and 5μM; 4h
Applications	β-Lapachone induced primarily S-phase arrest in SW480 cells, late S- and G2/M-phase arrest in SW620 cells, and early S-phase arrest in DLD1 cells. The cell cycle alterations were concentration-dependent. At 2.5μM, β-Lapachone induced S-phase arrest in all cell lines. When the concentration was increased to 5μM, more SW480 cells were arrested in S phase (53.1% at 5μM as compared to 43% at 2.5μM and 34.5% at control), more SW620 cells were arrested in S/G2 phase (93.7% at 5μM as compared to 64.5% at 2.5μM and 56.6% at control), and more DLD1 cells were arrested in early S phase.

Animal experiment [2]:

Animal models	Male Balb/c mice

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Preparation Method	After 1 week of acclimation, the mice were randomly allocated to one of the following groups (5 per group): control, β-Lapachone, cisplatin (18mg/kg, i.p.), and β-Lapachone + cisplatin (18mg/kg, i.p.). The β-Lapachone groups were fed a diet containing the drug (0.066%) for 2 weeks before cisplatin injection. All mice were sacrificed under carbon dioxide anesthesia 3 days after cisplatin injection. The blood samples obtained from the retro-orbital plexus were subjected to serum blood urea nitrogen (BUN) and creatinine (CRE) analyses. Half of the kidney was quickly removed for histopathological and immunohistochemical (IHC) studies. The other half was stored at -70°C until the western blot assay.
Dosage form	0.066%; orally
Applications	In the cisplatin-alone group, renal function was disrupted, and Mre11-Rad50-Nbs1 (MRN) complex expression increased. β-Lapachone co-treatment attenuated cisplatin-induced pathologic alterations. Although β-Lapachone markedly decreased cisplatin-induced renal cell apoptosis and DNA double-strand breaks (DSBs) formation, the β-Lapachone + cisplatin group showed the highest MRN complex expression. Moreover, β-Lapachone treatment increased the basal expression level of the MRN complex, which was accompanied by enhanced basal expression of SIRTuin1.

References:

[1] Huang L, Pardee AB. beta-lapachone induces cell cycle arrest and apoptosis in human colon cancer cells. *Mol Med*. 1999;5(11):711-720.
[2] Kim TW, Kim YJ, Kim HT, et al. ?-Lapachone enhances Mre11-Rad50-Nbs1 complex expression in cisplatin-induced nephrotoxicity. *Pharmacol Rep*. 2016;68(1):27-31.

Background

β-Lapachone is an ortho-naphthoquinone natural product, promoting several biological effects, such as anti-inflammatory, antibacterial, and anti-Trypanosoma, and β-Lapachone can inhibit topoisomerase I and induce NAD(P)H: quinone oxidoreductase 1[1-3].

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In vitro, after colon cancer cells SW480 cells were transiently exposed to β-Lapachone (2.5 or 5μM) for 4h, β-Lapachone induced primarily S-phase arrest in SW480 cells in a concentration-dependent manner[4]. Treatment of human hepatocellular carcinoma SK-Hep1 cells with different concentrations of β-Lapachone (1, 2, 4μM) for 18h showed that β-Lapachone increased the morphological appearance of dying cells in a dose-dependent manner, and cell viability was decreased in β-Lapachone-treated cells; furthermore, β-Lapachone also increased propidium iodide (PI) uptake (loss of plasma membrane integrity) in a dose-dependent manner[5].

In vivo, male Balb/c mice fed a diet containing β-Lapachone (0.066%) for 2 weeks before cisplatin injection (18mg/kg; i.p.), β-Lapachone markedly decreased cisplatin-induced renal cell apoptosis and DNA double-strand breaks (DSBs) formation, which was accompanied by enhanced basal expression of SIRTuin1, and the β-Lapachone + cisplatin group showed the highest Mre11-Rad50-Nbs1 (MRN) complex expression[6]. Log-phase A549 cells were injected subcutaneously into the flanks of athymic nude mice, followed by β-Lapachone (30mg/kg) injection through the tail vein, and β-Lapachone demonstrated potent in vivo antitumor activity with Tumor growth inhibition (TGI) = 70.1% and tumor proliferation rate (T/C) = 29.5%[7].

References:
[1] Gong Q, Hu J, Wang P, et al. A comprehensive review on β-lapachone: Mechanisms, structural modifications, and therapeutic potentials. *Eur J Med Chem*. 2021;210:112962.
[2] Ferraz da Costa DC, Pereira Rangel L, Martins-Dinis MMDDC, et al. Anticancer Potential of Resveratrol, β-Lapachone and Their Analogues. *Molecules*. 2020;25(4):893.
[3] Gomes CL, de Albuquerque Wanderley Sales V, Gomes de Melo C, et al. Beta-lapachone: Natural occurrence, physicochemical properties, biological activities, toxicity and synthesis. *Phytochemistry*. 2021;186:112713.
[4] Huang L, Pardee AB. beta-lapachone induces cell cycle arrest and apoptosis in human colon cancer cells. *Mol Med*. 1999;5(11):711-720.
[5] Park EJ, Min KJ, Lee TJ, Yoo YH, Kim YS, Kwon TK. β-Lapachone induces programmed necrosis through the RIP1-PARP-AIF-dependent pathway in human hepatocellular carcinoma SK-Hep1 cells. *Cell Death Dis*. 2014;5(5):e1230.
[6] Kim TW, Kim YJ, Kim HT, et al. β-Lapachone enhances Mre11-Rad50-Nbs1 complex expression in cisplatin-induced nephrotoxicity. *Pharmacol Rep*. 2016;68(1):27-31.
[7] Li X, Bian J, Wang N, et al. Novel naphtho[2,1-d]oxazole-4,5-diones as NQO1 substrates with

improved aqueous solubility: Design, synthesis, and in vivo antitumor evaluation. *Bioorg Med Chem*. 2016;24(5):1006-1013.