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Lapachone

National Cancer Institute

Source

National Cancer Institute. *Lapachone*. NCI Thesaurus. Code C28694.

A poorly soluble, ortho-naphthoquinone with potential antineoplastic and radiosensitizing activity. Beta-lapachone (b-lap) is bioactivated by NAD(P)H:quinone oxidoreductase-1 (NQO1), creating a futile oxidoreduction that generates high levels of superoxide. In turn, the highly reactive oxygen species (ROS) interact with DNA, thereby causing single-strand DNA breaks and calcium release from endoplasmic reticulum (ER) stores. Eventually, the extensive DNA damage causes hyperactivation of poly(ADP-ribose) polymerase-1 (PARP-1), an enzyme facilitating DNA repair, accompanied by rapid depletion of NAD⁺/ATP nucleotide levels. As a result, a caspase-independent and ER-stress induced mu-calpain-mediated cell death occurs in NQO1-overexpressing tumor cells. NQO1, a flavoprotein and two-electron oxidoreductase, is overexpressed in a variety of tumors.