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THE DNA TOPOISMERASE I INHIBITOR β-LAPACHONE INHIBITS PROLIFERATION AND DOWNREGULATES CYCLOOXYGENASE-2 GENE EXPRESSION IN HUMAN PROSTATE CARCINOMA CELLS

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Cyclooxygenases (COXs) are key enzymes in the conversion of arachidonic acid into prostanoids, which are involved in cell proliferation and inflammation. Two distinct COXs have been identified: COX-1 which is constitutively expressed and COX-2 which is induced by different products such as tumor promoters or growth factors. Previous studies have been demonstrated that DNA topoismerase I inhibitor β-lapachone , the product of a tree (Tabebuia avellanedae) from South America, strongly inhibits cell growth and induces apoptosis in various cancer cells. In this study, we investigated the effect of β-lapachone on the proliferation and COX expression in the human prostate carcinoma DU145 cell line. β-lapachone treatment caused an inhibition of DU145 cell growth and apoptosis induction which was associated with up-regulation of Bax and down-regulation of COX-2 but not COX-1 mRNA levels in a concentration-dependent manner; this is the first indication that β-lapachone selectively inhibits COX-2 gene expression. Our findings suggest a possible mechanism for the chemopreventive and anti-proliferative effects of β-lapachone.

keyword : β-lapachone, apoptosis, bax, cyclooxygenase