題名:Dihydrolipoic acid inhibits skin tumor promotion through anti-inflammation and anti-oxidation

作者:何元順
Yuan-Soon Ho; Ching-Shu Lai; Hsin-I Liu; Sheng-Yow Ho; Chein Tai; Min-Hsiung Pan; Ying-Jan Wang

貢獻者:醫學檢驗暨生物技術學系

上傳時間:2009-08-25T02:38:08Z

摘要:a-Lipoic acid (LA) has been intensely investigated as a therapeutic agent for several diseases, including hepatic disorder and diabetic polyneuropathy. However, the effects of LA or its reduced form, dihydrolipoic acid (DHLA), on cancer chemoprevention has never been reported. In the present study, we examined the effects of DHLA/LA on the production of nitric oxide (NO) by inducible NO synthase (iNOS) and the formation of prostaglandin E2 (PGE2) by cyclooxygenase-2 (COX-2), two important mediators associated with inflammation. DHLA/LA significantly inhibited lipopolysaccharide (LPS)-induced NO and PGE2 formation in RAW 264.7 cells. Meanwhile, treatment with DHLA/LA suppressed the expression of iNOS protein but, unexpectedly, did not affect or increase the expression of COX-2 protein. The in vivo anti-inflammatory and antitumor-promoting activities were evaluated by a topical 12-O-tetradecanoylphorbol 13-acetate (TPA) application to mouse skin withmeasurement of edema formation, epidermal thickness and hydrogen peroxide production. DHLA significantly inhibited the priming and activation stages of skin inflammation induced by a double TPA application, by decreasing the inflammatory parameters. Furthermore, DHLA inhibited DMBA (0.3 mmol)/TPA (2.0

nmol)-induced skin tumor formation
by reducing the tumor incidence and tumor multiplicity. When applied topically
onto the shaven backs of mice prior to TPA, DHLA markedly inhibited the expression of
iNOS protein. DHLA also strongly and directly inhibited COX-2 activity. These results
suggest that DHLA can be a possible chemopreventive agent in inflammation-associated
tumorigenesis.