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Suppression of DMBA/TPA-Induced Skin Tumorigenesis by Menthol through Inhibition of Inflammation, NF-kappaB, Ras-Raf-ERK Pathway

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Abstract : Growing evidence has shown that menthol has potent anticancer activity in various human cancers. However, its effect on skin cancer remains largely unknown. In the present study, we investigated the chemopreventive potential of menthol against 7, 12-dimethylbenz[a] anthracene(DMBA)/12-O-tetradecanoylphorbol 13-acetate (TPA)-induced skin tumorigenesis in ICR mice. Our results showed that menthol significantly inhibited TPA-induced inflammatory responses and pro-inflammatory cytokine release. We also found that menthol treatment significantly inhibited TPA-induced lipid peroxidation (LPO), mouse UDP-glucumno-syltransferase (UGT), mouse NADH Dehydrogenase, Quinone 1 (NQO1) release. Furthermore, we found menthol treatment significantly inhibited the tumor incidence and number of tumors ($P < 0.001$). Interestingly, we observed that menthol treatment significantly inhibited TPA-induced altered activity of NF-κB in skin tumor. Consistently, menthol-treated tumors also showed significantly suppressed the Ras-Raf-ERK signaling pathway. Thus, our results suggest that menthol inhibits DMBA/TPA-induced skin tumorigenesis by attenuating the Ras and inhibiting NF-κB activity via inhibition of inflammation responses and pro-inflammatory cytokine release.

Keywords : DMBA/TPA, NF-κB, Ras-Raf-ERK, skin tumorigenesis
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