Inhibition of carcinogen induced c-Ha-ras and c-fos proto-oncogenes expression by dietary curcumin

ABSTRACT

Whereas earlier work demonstrated that topical application of curcumin to mouse skin inhibited TPA-induced expression of c-fos, c-jun and c-myc oncogenes, our results are the first to show that orally consumed curcumin significantly inhibited DMBA- and TPA-induced ras and fos gene expression in mouse skin.

INTRODUCTION

Background Curcumin is yellow coloring matter isolated from roots of Curcuma longa Linn commonly called turmeric. It has been widely used in many Asian countries as a spice, to color cheese and butter, as a cosmetic and in some medicinal preparations. Curcumin (diferuloylmethane), a phenolic compound, possesses antioxidant, free radical scavenger and anti-inflammatory properties. Several works in epidemiology and animal model studies demonstrated that compounds which possess antioxidant or anti-inflammatory properties can inhibit carcinogenesis. One of the classic models is the inhibition of 12-0-tetradecanoylphorbol-13-acetate (TPA)-induced tumor promotion in mouse skin. TPA is a strong promoter of chemically induced skin cancer. It has been shown that TPA-induced skin tumors were inhibited by topical application of curcumin. Curcumin can inhibit the activity of cytochrome P450 and increase GSH content in rat liver which help to explain anticarcinogenic, antimutagenic and cytoprotective effects of curcumin. Many reports have shown that curcumin inhibits a variety of biological activities of TPA, which induces several biosynthetic processes, namely induction of ornithine decarboxylase, elevation or translocation of protein kinase C, induction of cyclooxygenase and lipooxygenase. Topical application of curcumin inhibits TPA-induced c-fos, c-jun, c-myc gene expression on mouse skin after 2 hours of TPA treatment. In present studies, we investigated the modulating effect of dietary curcumin on DMBA and TPA-induced tumor formation and on the expression levels of ras-p21 and fos-p62 to provide an understanding of the molecular basis of the relationship between the dietary curcumin and transforming function of oncogenic ras and fos during multi-stage skin carcinogenesis.

CONCLUSION

Kakar and Roy demonstrated that topical application of curcumin on mouse skin inhibited TPA induced expression of c-fos, c-jun and c-myc oncogene. Our results are the first report which demonstrate that dietary curcumin significantly inhibited DMBA- and TPA-induced ras and fos gene expressions in mouse skin. Curcumin may block a certain point on the signal transduction pathway leading to fos and ras oncogene expression.