

Bitter gourd (*Momordica charantia*): A potential mechanism in anti-carcinogenesis of colon

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TO THE EDITOR

Bitter gourd (*Momordica charantia*), has received widespread attention in the scientific community due to its beneficial effects, including anti-diabetic, anti-cancer and anti-inflammatory effects in laboratory studies^[1]. However, a well-defined mechanism by which this important plant food exerts its beneficial effects has not been elucidated. We present some of the latest findings on the plant's effects against colon cancer.

Bitter gourd seeds are enriched with 9c 11t 13t (9 *cis*, 11 *trans*, 13 *trans*) conjugated linolenic acid (CLN)^[2]. CLN collectively refers to a group of linolenic acid (18:3; c9, c11, c13) derivatives with positional (double bonds in carbon 9, 11 and 13 or 8, 10 and 12) and geometric (*cis*, *Z* and *trans*, *E*) isomers. Interestingly, 9c 11t 13t CLN-enriched bitter gourd seed extracts protect colon from chemical-induced carcinogenesis in rats^[3]. The fatty acid significantly reduced the incidences as well as multiplicity of colonic adenocarcinoma. In a separate, short-term study, bitter gourd seed oil significantly reduced the number and frequency of aberrant crypt foci (ACF) in the colon of male F-344 rats treated with azoxymethane^[4]. *In vitro*, bitter gourd seed oil inhibits proliferation and induces apoptosis of human colon carcinoma DLD-1 and HT-29 cells^[5,6].

In an attempt to elucidate a possible receptor-mediated mechanism of anti-carcinogenesis, bitter gourd seed oil has been shown to increase the expression of peroxisome

proliferator-activated receptor gamma (PPAR γ), a member of nuclear hormone receptor superfamily^[7]. Furthermore, 9c 11t 13t CLN activated PPAR γ in transfection experiments^[8], its effect comparable to BRL-49653, a specific ligand for PPAR γ . These important studies indicate that bitter gourd's effect in the colon may be mediated in part by PPAR γ .

Functionally, PPAR is a ligand-activated transcription factor, which is involved in gene expression in a tissue-, sex- and species-dependent manner. Upon activation, PPAR forms a heterodimer with RXR α and regulates gene expression by binding to PPAR-response elements (PPRE) on responsive genes. Target genes for PPAR include lipid metabolizing enzymes and growth regulatory genes. To date, three subtypes of PPAR (α , β and γ) have been identified in several species including human^[9].

PPAR γ is highly expressed in normal human colon and colon tumors as well as cell lines derived from colon cancer^[10]. Expression of this receptor subtype in colon cells has been found equal to or even greater than adipose tissue, where it was originally characterized^[10]. PPAR γ activation has been shown to inhibit cell growth, promote differentiation and stabilize genes that are altered in colon cancer^[10-12]. The current prevailing belief is that PPAR γ 's ability to enhance differentiation and apoptosis is a positive event, associated with cell-cycle arrest and reduced proliferation^[12]. Similar beneficial effects (growth inhibition, induction of apoptosis) were observed with bitter gourd against colon carcinogenesis^[3-7].

Taken together, there is an association of PPAR γ in CLN-mediated effects in the colon. Further studies are required to understand the detailed mechanism.

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