RESEARCH COMMUNICATION

Oral Consumption of Bitter Gourd and Tomato Prevents Lipid Peroxidation in Liver Associated with DMBA Induced Skin Carcinogenesis in Mice

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Abstract

The protective role of two commonly consumed natural dietary items- bitter gourd and tomato against endogenous as well as 7,12- dimethylbenz(a)anthracene (DMBA) induced lipid peroxidation in the livers of mice was investigated. The rationale for such an approach is that lipid peroxidation has been suggested to play a key role in human cancer development. There was a sharp rise in lipid peroxidation (measured as thiobarbituric acid reactive substances formation) during skin carcinogenesis induced by DMBA in mice. Aqueous extracts of bitter gourd and tomato juice were found to be very potent inhibitors of lipid peroxidation both in normal and DMBA treated mice. Our observations support the hypothesis that natural combinations of phytochemicals present in the fruit juices exert cancer-protective effects via a decrease in lipid peroxidation.

Key words: DMBA, bitter gourd, tomato, lipid peroxidation, mouse liver

Introduction

Lipid peroxidation is a normal biochemical process which involves oxidation of polyunsaturated fatty acids (PUFAs) as components of cell membranes. Elevated lipid peroxidation can result in generation of various reactive oxygen species and has been associated with tissue injury due to damage of cellular macromolecules, including DNA. Lipid hydroperoxides (LHPs) are toxic to cells because they decrease membrane fluidity and permeability and ultimately result in cell lysis (Tappel, 1973., Inouye, 1984., Niki et al., 1991). Because of this, lipid peroxidation has been suggested to play a key role in human cancer development (Wiseman and Halliwell, 1996).

Bitter gourd (Momordica charantia Linn), a cucurbitaceae fruit, is commonly consumed as a vegetable in India and other Asian countries. It is recognized to be of medicinal value in the Indian system of medicine and the fruit juice is considered to be a tonic for the stomach with application for diseases of the liver and spleen (Ambasta, 1992). Chemical studies showed that bitter gourd contains glycosides, saponins, alkaloids, reducing sugars, resins, phenolic constituents, fixed oil and free acids (Dhalla et al., 1961). Momordica charantia has been reported to possess antimutagenic properties which is attributed to the presence of specific acylglucosylsterols (Guevara et al., 1990). Regarding influence on skin carcinogenesis, Singh et al (1998) noted the inhibitory potential of Momordica charantia peel, pulp, seed and whole fruit extract during the peri-initiation stage (1 week before and 2 weeks after initiation) and/or during the tumour promotion stage and noted reduction in DMBA induced tumour burden. We also observed that oral administration of the aqueous fruit extract can protect against DMBA induction of skin tumours in mice (De, 1999).

Tomato (Lycopersicon esculentus), a member of the Solanaceae, is consumed widely as a vegetable and as an appetizer (juice and ketchup). Active compounds isolated from tomato that have anticarcinogenic properties include...
cholorogenic acid, eugenol, quercetin, rutin, kaempferol, naringenin, alpha and beta carotenes, phytoene, neurosporene and lycopene (Beecher, 1995). A recent population study has established a close link between dietary intake of tomatoes, a major source of the antioxidant carotenoid lycopene, and lowered risk of cancer (Rao and Agarwal, 1998). Epidemiological studies have also revealed beneficial effects of tomato against cancers of pancreas, colon, rectum, esophagus, oral cavity, breast and cervix, though it is more effective against prostate, lung and stomach cancers (Giovannucci, 1999). Significant reduction, both in lesion number and size of DMBA induced rat mammary tumours, was observed following treatment with lycopene-enriched tomato oleoresin (Sharoni et al., 1997). Reduction in incidence and progression of DMBA induced skin papillomas due to oral tomato juice has also been noted (De, 1999).

In view of the growing interest in the search for food and diet-related means of preventing carcinogenesis, the present study was conducted to assess the role of aqueous extract of bitter gourd and tomato juice on lipid peroxidation in liver induced by dimethylbenzanthracene (DMBA), a compound that is capable of binding to DNA, RNA and other macromolecules and induce carcinogenesis.

Materials and Methods

Materials

Bitter gourd and tomato were obtained fresh from local markets. 7,12-dimethylbenzantrachene (DMBA), sodium dodecyl sulphate (SDS), thiobarbituric acid (TBA) and pyridine were purchased from Sigma Chemicals, USA. Acetic acid, n-butanol and potassium chloride were obtained from E. Merck, India.

Experimental Animals

Swiss albino female mice, weighing 20-24 g in the age group of 4-5 weeks were supplied by the animal colony of our institute. The animals were maintained in groups of 5 per cage with alternating periods of light and dark of 12 hours each. Standard animal food pellets (Lipton India Ltd) and water were provided ad libitum.

Preparation of test substances

DMBA was dissolved in 1% DMSO. Fruit of bitter gourds was extracted in an electrically operated mixer/grinder and diluted with distilled water (1:20). The solution was allowed to stand and the supernatant strained through a fine muslin cloth. Tomato juice was prepared in the grinder mixer and diluted with distilled water (1:2).

Treatment groups: Group1: Normal mice receiving distilled water only in place of bitter gourd extract or tomato juice. Group2: Normal mice receiving oral administration of bitter gourd (50ml/mouse/day) or tomato juice (100ml/mouse/day) throughout the experimental period (2 months). The treatment doses were selected on the basis of our previous observation and these were the minimal effective doses for reduction of tumour incidence. Group3: Mice receiving 3 topical applications of 1% DMBA on alternate days followed by croton oil (1%) applied twice weekly for 2 months. Group4: Mice receiving bitter gourd extract or tomato juice daily, simultaneously with carcinogen administration.

Results

Considerable elevation of lipid peroxides was noted following carcinogen administration (P<0.001). Oral intake of both bitter gourd extract and tomato juice was found to reduce the level of lipid peroxides significantly (P<0.001) both in normal and carcinogen-treated groups (Figures 1 and 2). The reduced lipid peroxidation in both cases was more striking in the carcinogen-treated groups.

Discussion

Considering the existing knowledge regarding carcinogenesis and anticarcinogens, we have undertaken studies to experimentally evaluate the role of selected fruits and other plant parts that are components of the human diet, in prevention of carcinogenesis and to understand their mechanisms of action. The present report documents our observations with two commonly consumed vegetables.

Inhibition of skin papillomagenesis by topical application of fruit extracts of Momordica charantia, widely consumed...
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by Asians, was earlier reported (Singh et al., 1998). We also noted that oral administration of bittergourd, instead of topical application, can significantly reduce the incidence of mouse skin papillomas, premalignant lesions, induced by a chemical carcinogen (De, 1999). The effect of oral feeding of bitter gourd extract (aqueous) was therefore studied on the levels of lipid peroxides in livers of both normal and carcinogen treated mice.

Interest in tomato as a natural package of anticarcinogenic agents was generated on the basis of the presence of a number of carotenoids besides lycopene (Beecher, 1995) and the observation that Mediterranean diet, which includes high amounts of tomato, is associated with low cancer risk (Ferro-Luzzi and Sette, 1989). Rao and Agarwal (1998) noted reduced serum thiobarbituric acid reactive substances by dietary supplementation of lycopene through tomato juice, spaghetti sauce and tomato oleores in healthy human subjects. Lycopene was shown to enhance gap junctional communication and suppress lipid peroxidation (Zhang et al., 1991). Here we demonstrated an inhibitory effect of oral tomato juice on the formation of lipid peroxides in liver.

Carcinogenesis is known to be enhanced by lipid peroxides by causing damage to cellular macromolecules. In this study we noted a sharp rise in lipid peroxides following administration of DMBA, especially which when followed by promotion induces skin papillomas and carcinomas in mice. Treatment with bitter gourd and tomato significantly reduced lipid peroxidation, either endogenous or DMBA induced, although to a greater extent in the latter case. It is most likely that the potential effect of aqueous extract of bitter gourd and tomato juice in reducing the lipid peroxide level is a consequence of the modulatory influence of the juices on the biotransformation enzymes of detoxification. Effects of bitter gourd on lipid peroxidation have not been reported earlier to our knowledge, and this study is perhaps the first observation of its kind to show inhibitory influence in the liver.

Prevention of cancer may be effected by multiple mechanisms, and one way by which anticarcinogens may act is by reducing lipid peroxidation. Fruits of bitter gourd and tomato contain a wide variety of potentially anticarcinogenic substances which are likely to exert synergistic effects in preventing carcinogenesis. As the present study revealed, one mechanism is to inhibit lipid peroxidation. It is clearly important to initiate a more extensive search to explore the anticarcinogenic role of other plant foods and determine their toxicity and effective dose levels, so that these agents may be considered for application in prevention of human carcinogenesis.

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**Fig 1. Effects of bitter gourd extract on lipid peroxidation.** Estimation was made with liver microsomal fractions from normal (N), normal + bitter gourd (N+B), carcinogen treated (C) and carcinogen + bitter gourd treated (C+B) animals. Data are means ± SE (n=8).

**Fig 2. Effects of tomato juice on lipid peroxidation.** Liver microsomal fractions were examined from normal (N), normal + tomato (N+T), carcinogen treated (C) and carcinogen + tomato treated (C+T) animals. Data are means ± SE (n=8).
**Personal Profile: Sukta Das**

Dr Sukta Das is a Senior Scientist and head of the Department of Cancer Chemoprevention at Chittaranjan National Cancer Institute in Calcutta. She has been engaged in cancer research for the last 30 years, working on aspects of tumour biology, host-tumour relationships, nutrition and cancer and most recently cancer chemoprevention.

Dr Das is also a Research Guide for Doctoral and Post-Doctoral scholars with major responsibilities for helping younger scientists develop their careers. She herself spent time as a visiting post-doc in London at the Imperial Cancer Research Fund, and has been the recipient of many research fellowships. A member of a number of learned societies and associations, Dr Das has contributed much in the way of editorial activities in different capacities, and is now serving as one of the Specialist Editors for Natural Products of the APJCP.

**References**


