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Lack of chemopreventive effects of ginger on colon carcinogenesis induced by 1,2-dimethylhydrazine in rats

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Abstract

Ginger (*Zingiber officinale* Roscoe) has been proposed as a promising candidate for cancer prevention. Its modifying potential on the process of colon carcinogenesis induced by 1,2-dimethylhydrazine (DMH) was investigated in male Wistar rats using the aberrant crypt foci (ACF) assay. Five groups were studied: Groups 1–3 were given four s.c. injections of DMH (40 mg/kg b.w.) twice a week, during two weeks, whereas Groups 4 and 5 received similar injections of EDTA solution (DMH vehicle). After DMH-initiation, the animals were fed a ginger extract mixed in the basal diet at 0.5% (Group 2) and 1.0% (Groups 3 and 4) for 10 weeks. All rats were killed after 12 weeks and the colons were analyzed for ACF formation and crypt multiplicity. The rates of cell proliferation and apoptosis were also evaluated in epithelial colonic crypt cells. Dietary consumption of ginger at both dose levels did not induce any toxicity in the rats, but ginger meal at 1% decreased significantly serum cholesterol levels ($p < 0.038$). Treatment with ginger did not suppress ACF formation or the number of crypts per ACF in the DMH-treated group. Dietary ginger did not significantly change the proliferative or apoptosis indexes of the colonic crypt cells induced by DMH. Thus, the present results did not confirm a chemopreventive activity of ginger on colon carcinogenesis as analyzed by the ACF bioassay and by the growth kinetics of the colonic mucosa.

Keywords: Dimethylhydrazine; Aberrant crypt foci; Colon carcinogenesis; Ginger; Chemoprevention

1. Introduction

Colorectal cancer is an important cause of death in the western world and, although its causes are not completely understood, it is generally accepted that hereditary genetic component, high fat diets and alcohol consumption are among the greatest risk factors (Lieberman et al., 2003; Jo and Chung, 2005). Thus, it is imperative to identify agents that could inhibit or minimize such cancer-inducing factors and, therefore, primary dietary prevention by fruits or other edible plants could play a role in the control of human colon carcinogenesis (Mason, 2002).

Development of rodent chemically induced colon cancer is a multi-step process involving a series of pathological alterations, ranging from discrete microscopic mucosal lesions like aberrant crypt foci (ACF) to malignant tumors (McLellan et al., 1991; Bird, 1995; Rodrigues et al., 2002; Yamada and Mori, 2003). The ACF are putative preneoplastic lesions in both rodent and human colon (Bird, 1995; Roncucci et al., 1991; Pretlow et al., 1991). The ACF can be easily induced in rat colon after administration of 1,2-dimethylhidrazine (DMH) or of azoxymethane (AOM). Their detection has been proposed as a biomarker in short and medium-term bioassays to evaluate

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chemopreventive agents in the rat (Pereira et al., 1994; Kawamori et al., 1995; Wargovich et al., 1996).

Many components of medicinal or dietary plants have been identified as possessing potential chemopreventive properties capable of inhibiting, retarding or reversing the multi-stage carcinogenesis process (Surh et al., 1998; Surh, 2002). Ginger, the branched rhizome of *Zingiber officinale* Roscoe (Zingiberaceae), is one of the most widely used spices, and is utilized as a condiment for a variety of compounded foods and beverages due to its characteristic aromatic and pungent flavor. Ginger extracts are rich in gingerols and shogaols, which exhibit anti-oxidant, anti-inflammatory, anti-fungical, anti-mycobacterial and anti-carcinogenic proprieties under "in vitro" and "in vivo" systems (Surh et al., 1998; Surh, 2002).

In folk medicine, ginger has been used traditionally as a carminative, diaphoretic, anti-spasmodic and anti-emetic agent against motion sickness and hyperemesis gravidarum (Langner et al., 1998). Some constituents of ginger have potent anti-oxidant and anti-inflammatory effects, and some of them exhibit anti-tumor activity in rodent skin and intestinal chemical carcinogenesis models (Katiyar et al., 1996; Yoshimi et al., 1992; Park et al., 1998; Surh et al., 1997). Pungent ginger ingredients such as [6]-gingerol and [6]-paradol have shown in vitro anti-tumor activity against different cell lineages (Lee and Surth, 1998; Keum et al., 2002).

As a number of natural compounds prevent colon carcinogenesis in rodents by inhibition of ACF development (Pereira et al., 1994; Kawamori et al., 1995; Wargovich et al., 1996; Bazo et al., 2002), the present study was designed to verify the potential protective influence of the dietary consumption of ginger extract against the development of colonic ACF in an experimental model of colon carcinogenesis induced by DMH in the rat. Furthermore, the rates of cell proliferation and apoptosis were also evaluated in epithelial colonic crypt cells.

2. Material and methods

2.1. Animals and treatment

Male 4-week-old Wistar rats were obtained from CEMIB (UNICAMP Campinas, SP, Brazil). The animals were kept in polypropylene cages (5 animals/cage) covered with metallic grids in a room maintained at 22 ± 2 °C, 55 ± 10% humidity and with a 12-h light-dark cycle. They were fed commercial Purina chow (LABINA, Paulínia, SP, Brazil) and water ad libitum for a 2-week acclimation period. Samples of lyophilized extract of ginger, obtained from hydroalcoholic extraction by spray dryer system containing approximately 2.54% gingerols as determined by HPLC method, were supplied generously by CentroFlora Group (Botucatu-SP, Brazil).

The University Ethical Committee for Animal Research approved the protocols used in this study (protocol no. 51/01).

2.2. Experimental design

The animals were randomly allocated into five groups (Fig. 1): Groups 1–3 were given four s.c. injections of DMH (40 mg/kg b.w.) twice a week, for two weeks; Groups 4 and 5 received similar injections of EDTA solution (DMH vehicle, 37 mg/100 ml distilled water). After initiation of colon carcinogenesis with DMH the animals were fed either basal diet (Groups 1 and 5) or a ginger extract mixed in the basal diet at 0.5% (Group 2) or 1.0% (Groups 3 and 4), respectively, for 10 weeks. Food and water consumption were measured twice a week throughout all the experimental period. The animals were weighed once a week.

At the end of the 12th week, all animals were killed. Two hours before killing, the animals received a single i.p. injection of 100 mg/kg b.w. of bromodeoxyuridine (BrdU) (Sigma Chemical Co.) between 8 a.m. and 10 a.m.

2.3. Tissue processing, histology and immunohistochemical proceedings

At necropsy, the liver, kidneys and colon (Groups G1–G5) and thymus, spleen, femur (bone marrow) and mesenteric lymph nodes (Groups

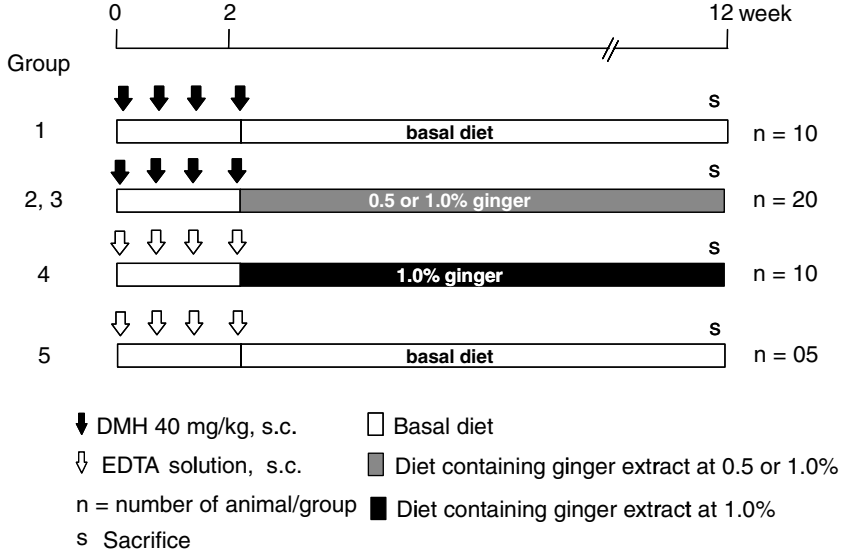

Fig. 1. Experimental design (for details see Section 2.2): (G1) DMH; (G2) DMH + 0.5% ginger; (G3) DMH + 1.0% ginger; (G4) 1.0% ginger; (G5) control.

G4 and G5) were removed, and weighed (liver, kidneys, spleen and thymus) and representative samples were fixed in 10% phosphate-buffered formalin solution for 48 h.

The entire colon was removed, longitudinally opened, rinsed with 0.9% NaCl solution and fixed flat in buffered formalin for 24 h. For ACF counting, middle and distal colons were stained with 1% methylene blue dissolved in phosphate-buffered salt solution (PBS) for 1 min. As the incidences and/or multiplicity of murine colon ACF, adenomas and adenocarcinomas are higher in the middle and distal colon than in the proximal colon of animals treated with DMH (Poten et al., 1992; Park et al., 1997; Rodrigues et al., 2002; Jackson et al., 2003) we focused our analysis only on the middle and distal portions of the colon.

Analysis and quantification of ACF (Fig. 2A) were performed according to Bird's criteria (1995). The number of ACF/colon and the number of aberrant crypts in each ACF were determined under light microscopy at 40× magnification. Colonic crypts overlaying lymphoid follicles were excluded from the score, since normal crypts in this area can occasionally be confused with aberrant crypts. After ACF analysis, samples of the middle and distal colon were cut into serial strips, processed for paraffin embedding, cut into 5-μm-thick sections and stained with hematoxylin-eosin for histological analysis. The avidin–biotin-peroxidase complex (ABC) method was employed for detection of nuclear BrdU incorporation (Hsu et al., 1981). Briefly, after deparaffination colon sections of 5 μm thickness over poly-L-lysine coated slides were treated sequentially with 2 N HCl for 20 min, 3% H_2O_2 in PBS for 10 min, non-fat milk for 60 min, anti-BrdU antibody (Sigma, EUA, dilution 1:200) overnight, biotinylated horse anti-mouse IgG (dilution 1:300) for 60 min and avidin–biotin-peroxidase solution (dilution 1:50) for 45 min (Elite ABC kit, Vector Laboratory, Burlingame, CA, EUA). Chromogen color development was accomplished with 3,3′-diaminobenzidine tetrahydrochloride (Sigma, EUA). Slides were counterstained with Harris's haematoxylin.

2.4. Proliferation and apoptosis indexes

At least 20 perpendicular well-oriented crypts from the distal and middle colon were examined in each animal under light microscopy at 400× magnification (Chang et al., 1997). The rate of colonic cell proliferation (BrdU LI%) was evaluated as the percentage of cells with BrdU-labeled nuclei (Fig. 2B) among the total number of counted cells in a perpendicular colonic crypt. The apoptosis index (AI%) was estimated as the percentage of apoptotic cells (i.e., with cellular retraction and condensation, condensed or fragmented nuclear chromatin and formation of apoptotic bodies) (Fig. 2C) among the total number of counted cells in a whole colonic crypt (Risio et al., 1996).

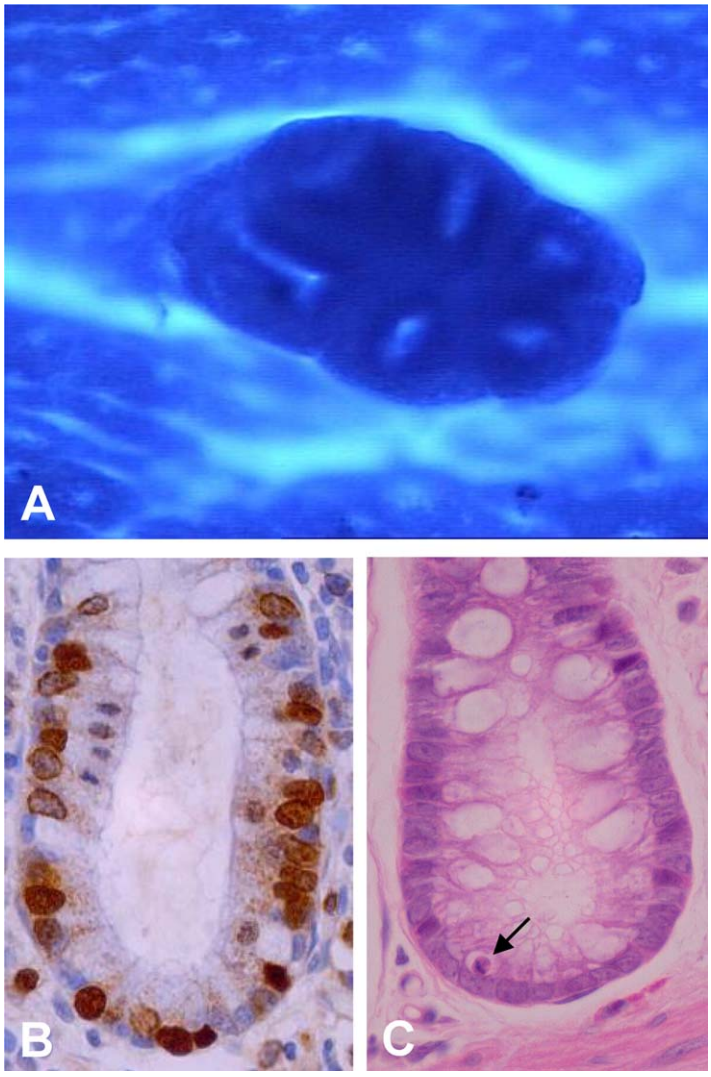

Fig. 2. Topographic view of one ACF with six altered crypts (A), BrdU labeling cells (B, dark nuclei) and apoptotic cell (C, arrow) in sectioned intestinal glands.

2.5. Hematological evaluation and serum biochemistry

Immediately before necropsy, whole blood was collected from the animals for serum total cholesterol (Groups G4 and G5), and alanine aminotransferase (ALT) and creatinine determination (Groups G1–G5). The analysis was carried out spectrometrically with the use of commercial kits (Bayer, France). Peripheral blood samples were collected for hematological analysis in Vacutainer tubes with 1.5% EDTA and differentially quantified through a Coulter T890 for the following: leukocyte, erythrocyte and platelet counts and hemoglobin determination (Groups G4 and G5).

2.6. Statistical analysis

The statistical analysis was done using the Jandel Sigma Stat software (Jandel Corporation, San Rafael, CA, USA). Body weight gain, relative liver and kidney weights, food consumption, BrdU labeling and apoptosis indexes, ACF development and multiplicity, and serum biochemistry data were analyzed by the ANOVA or Kruskal–Wallis tests. Hematological and serum total cholesterol and relative thymus and spleen weight data were analyzed by the *t*-test. Significant differences were assumed when $p < 0.05$.

3. Results

3.1. General observations

All rats survived until the end of the experiment. DMH initiation and ginger treatment were well accepted by the animals. Ginger extract meal at 0.5% and 1.0% did not change body-weight gain (Table 1). At the lifetime of post-initiation period (weeks 3–12) food consumption was significantly higher ($p < 0.01$) in the ginger-treated groups (G2, G3 and G4) than in the respective untreated control groups (G1 and G5) as shown in Table 1. At the end of the experiment, neither absolute nor relative liver and kidneys weights and ALT and creatinin serum levels were modified by ginger treatment (Table 2).

To analyze a possible adverse effect of ginger treatment per se, some biochemical and hematological parameters and lymphoid organs (weight and histology) were evaluated only in Groups 4 and 5. Relative thymus and spleen weights (Table 3) and histology of thymus, spleen, bone marrow (femur) and mesenteric lymph nodes were not altered by ginger treatment. The total cholesterol serum levels were significantly decreased by the 1.0% ginger extract meal (G4 vs. G5, $p < 0.038$) (Table 3).

Table 3
Relative thymus and spleen weights and hematological and biochemical analysis from 1.0% ginger-treated (G4) and control (G5) groups[a]

Parameters	Experimental groups[b]	
	Ginger 1.0% (G4)[c]	Control (G5)
Relative weight		
Thymus	0.10 ± 0.02	0.11 ± 0.03
Spleen	0.24 ± 0.04	0.23 ± 0.02
Hematological/biochemical analysis		
Hemoglobin (g/dL)	13.70 ± 0.20	13.63 ± 0.43
Total plasmatic protein (g/dL)	5.64 ± 0.17	5.47 ± 0.28
Total cholesterol (mg/dL)	68.80 ± 13.65*	86.40 ± 14.50
Red blood cells ($\times 10^6$/μL)	7.69 ± 0.35	7.44 ± 0.32
Leucocytes ($\times 10^3$/μL)	2.28 ± 0.60	2.71 ± 0.98
Plaquets ($\times 10^5$/μL)	6.42 ± 1.17	6.30 ± 1.85

* Statically different from control group (G4 vs. G5), $p < 0.038$.
[a] Values are mean ± SD.
[b] Ginger = *Zingiber officinale* Roscoe extract at 1.0% in basal diet for 10 weeks.
[c] Number of animals analyzed.

Table 1
Initial and final body weights, body-weight gain, food and ginger consumption in the different experimental groups[a]

Group/treatment[b]	Number of rats	Initial body weight (g)	Final body weight (g)	Body-weight gain[c] (g)	Food consumption (g/rat/day)[c]	Ginger consumption (g/rat/day)[c]
(G1) DMH	10	270.7 ± 13.3	431.4 ± 29.2	160.7 ± 21.7	23.7 ± 1.3	–
(G2) DMH + 0.5% ginger	10	277.5 ± 12.7	447.4 ± 22.1	169.9 ± 14.8	25.0 ± 2.0*	0.13 ± 0.01
(G3) DMH + 1.0% ginger	10	281.9 ± 14.7	450.2 ± 32.5	168.3 ± 22.9	26.2 ± 2.0*	0.26 ± 0.02
(G4) 1.0% ginger	10	289.5 ± 15.9	441.6 ± 26.4	162.1 ± 11.0	25.4 ± 1.8*	0.25 ± 0.02
(G5) Control	05	271.0 ± 19.5	433.6 ± 11.8	162.6 ± 9.4	22.7 ± 1.0	–

* Statically different from control group (G2, G3 and G4 vs. G1 and 5), $p < 0.01$.
[a] Values are mean ± SD.
[b] DMH = 1,2-dimethylhydrazine (4 × 40 mg/kg, s.c.); ginger = *Zingiber officinale* Roscoe extract at 0.5% and 1.0% in basal diet during 10 weeks.
[c] From the 3rd to the 12th week of the experiment.

Table 2
Liver and kidney relative weights (%), alanine aminotransferase (ALT) and creatinin serum levels in the different groups[a]

Group/treatment[b]	Number of rats	Liver relative weight	ALT (U/L)	Kidney relative weight		Creatinin (mg/dL)
				Right	Left	
(G1) DMH	10	3.24 ± 0.15	48.40 ± 6.22	0.29 ± 0.02	0.27 ± 0.01	0.43 ± 0.04
(G2) DMH + 0.5% ginger	10	3.33 ± 0.25	50.80 ± 14.57	0.29 ± 0.02	0.27 ± 0.02	0.43 ± 0.05
(G3) DMH + 1.0% ginger	10	3.20 ± 0.19	49.00 ± 10.64	0.29 ± 0.02	0.27 ± 0.02	0.50 ± 0.13
(G4) 1.0% ginger	10	3.32 ± 0.37	48.20 ± 4.85	0.29 ± 0.01	0.27 ± 0.02	0.50 ± 0.09
(G5) Control	05	3.36 ± 0.28	47.40 ± 4.36	0.30 ± 0.02	0.29 ± 0.02	0.49 ± 0.05

[a] Values are mean ± SD.
[b] DMH = 1,2-dimethylhydrazine (4 × 40 mg/kg b.w., s.c.); ginger = *Zingiber officinale* Roscoe extract at 0.5% and 1.0% in basal diet during 10 weeks.

3.2. ACF development and colonic BrdU-labeling and apoptosis indexes

The numbers of ACF and crypt multiplicity in the middle and distal colon in the different groups are summarized in Table 4. All DMH-initiated animals (Groups G1–G3) developed ACF as analyzed at the 12th week of the experiment. Treatment with ginger extract did not suppress ACF formation or crypt multiplicity induced by DMH in the middle and distal colon when compared with the respective initiated group (G1). Values for total aberrant crypt and total aberrant crypt foci were observed to be higher in the DMH-initiated and 1.0% ginger-treated group (G3) than in other DMH-initiated groups, although not to statistically significant extent ($0.05 < p < 0.1$).

The colonic BrdU labeling and apoptosis indexes are shown in Table 5. The DMH-initiated group (G1) presented a significant increase in the rate of colonic cell proliferation (BrdU PI%) when compared to the respective non-initiated control group (G5) ($p < 0.05$). Ginger meal reduced BrdU LI% in the middle and distal colon of DMH-initiated groups, especially in the group that received 0.5% ginger, although the reduction was not statistically significant (G1 vs. G2 and G3, $0.05 < p < 0.1$).

Dietary ginger at both dose levels did not change the apoptotic indexes of the colonic crypts in the DMH-initiated or non-initiated groups (G1 vs. G2 and G3; G4 vs. G5) in the middle and distal colon as shown in Table 5.

4. Discussion

The present study was undertaken to investigate whether ginger given by diet after carcinogen treatment can modify colon carcinogenesis in rats, as evaluated by

Table 4
Effect of ginger extract on aberrant crypt foci (ACF) and crypt multiplicity (crypt/ACF) in the middle and distal colon[a]

Group/treatment[b]	Number of rats	Number of aberrant crypts per ACF				Total number AC[c]	Total number ACF	Crypt/ACF
		1 crypt	2 crypts	3 crypts	⩾4 crypts			
Middle colon								
(G1) DMH	10	26.2 ± 29.7	29.0 ± 24.3	22.0 ± 11.0	11.5 ± 6.0	226.8 ± 195.1	95.6 ± 85.4	2.3 ± 0.3
(G2) DMH + 0.5% ginger	10	18.6 ± 10.6	22.6 ± 8.9	19.5 ± 12.0	8.0 ± 5.0	151.1 ± 70.8	73.8 ± 23.1	2.1 ± 0.7
(G3) DMH + 1.0% ginger	10	40.7 ± 22.5	38.9 ± 16.7	21.0 ± 17.0	22.0 ± 13.0	303.1 ± 211.3	135.2 ± 65.0	2.1 ± 0.8
(G4) 1.0% ginger	10	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.3	0.4 ± 1.3	0.1 ± 0.3	0.4 ± 1.3
(G5) Control	05	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Distal colon								
(G1) DMH	10	22.7 ± 18.5	35.2 ± 30.4	22.2 ± 16.1	9.1 ± 6.9	197.9 ± 145.5	89.2 ± 67.8	2.3 ± 0.4
(G2) DMH + 0.5% ginger	10	17.2 ± 11.9	28.2 ± 12.1	17.2 ± 11.6	6.9 ± 8.5	153.8 ± 90.5	69.5 ± 35.3	2.1 ± 0.3
(G3) DMH + 1.0% ginger	10	24.7 ± 21.0	37.0 ± 27.5	29.0 ± 19.2	19.0 ± 14.5	268.3 ± 175.4	109.7 ± 81.2	2.5 ± 0.4
(G4) 1.0% ginger	10	0.1 ± 0.3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.3	0.1 ± 0.3	0.1 ± 0.3
(G5) Control	05	0.2 ± 0.4	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.2 ± 0.4	0.2 ± 0.4	0.2 ± 0.4

[a] Values are mean ± SD.
[b] DMH = 1,2-dimethylhydrazine (4 × 40 mg/kg b.w., s.c); ginger = *Zingiber officinale* Roscoe extract at 0.5% and 1.0% in basal diet during 10 weeks.
[c] AC = aberrant crypt.

Table 5
BrdU labeling (BrdU LI%) and apoptosis (AI%) indexes in the middle and distal colon[a]

Group/treatment[b]	Number of rats	Growth kinetics			
		BrdU LI%		AI%	
		"Normal-appearing" crypts	Normal crypts	"Normal-appearing" crypts	Normal crypts
Middle colon					
(G1) DMH	10	10.25 ± 3.70*	–	1.42 ± 0.68	–
(G2) DMH + 0.5% ginger	10	6.92 ± 3.36	–	0.93 ± 0.62	–
(G3) DMH + 1.0% ginger	10	7.95 ± 3.10	–	1.35 ± 0.76	–
(G4) 1.0% ginger	10	–	5.35 ± 1.15	–	1.46 ± 0.74
(G5) Control	05	–	4.77 ± 0.88	–	1.59 ± 0.86
Distal colon					
(G1) DMH	10	8.00 ± 2.25	–	1.22 ± 0.41	–
(G2) DMH + 0.5% ginger	10	5.11 ± 1.47	–	0.98 ± 0.62	–
(G3) DMH + 1.0% ginger	10	5.92 ± 1.36	–	1.84 ± 0.97	–
(G4) 1.0% ginger	10	–	5.84 ± 1.26	–	1.57 ± 0.74
(G5) Control	05	–	4.28 ± 1.19	–	1.11 ± 0.22

* Statically different from control group (G1 vs. G5), $p < 0.05$.
[a] Values are mean ± SD.
[b] DMH = 1,2-dimethylhydrazine (4 × 40 mg/kg b.w., s.c.); ginger = *Zingiber officinale* Roscoe extract at 0.5% and 1.0% in basal diet during 10 weeks.

the ACF bioassay. The results showed that dietary ginger did not suppress the development of ACF and crypt multiplicity at both dose levels tested. These results indicate that ginger was not able to suppress the clonal expansion of DMH initiated cells in the colonic mucosa. It is possible that ginger could not substantially reach to the lumen of the colon and exert its chemopreventive effects due to absorption in the small intestine. Our results on the reduction of cholesterol serum levels in the groups that received ginger suggest that it is absorbed in the small intestine. Yoshimi et al. (1992) reported that dietary administration of 0.02% gingerol during the initiating phase of intestinal carcinogenesis by azoxymethane inhibited the multiplicity of adenocarcinomas (tumor burden) in Fischer 344 rats after 20 weeks. This inhibiting effect was observed with regard to the entire intestine, however, when only the large intestine was considered, this protective influence was not observed for the development of colon tumors.

Our group has published some studies on chemoprevention of colon carcinogenesis using the ACF medium-term bioassay (Agner et al., 2005; de Lima et al., 2005; Bazo et al., 2002). Various studies have strongly suggested that ACF, particularly dysplastic ACF or β-catenin positive ACF, are precursor lesions of colon cancer in humans and rodents (Mori et al., 2005; Takayama et al., 2005). However, some contradictory findings between rodent short-term (ACF end-point) and long-term experiments (tumor end-point) have been reported (Hardman et al., 1991; Steele et al., 1995; Rao et al., 1997; Wijnands et al., 2005). For example, the ability of genistein to inhibit colon carcinogenesis has been inconclusive or contradictory (Steele et al., 1995; Rao et al., 1997; Thiagarajan et al., 1998; Gee et al., 2000). The possibility exists that some false-positive or false-negative results between ACF and colon tumors end-points may occur due to the multi-factorial nature of the process of colon carcinogenesis. Thus, an effective influence of ginger on colon carcinogenesis should continue to be investigated mainly in long-term treatments.

Recent studies suggest that the in vitro anti-tumor effects of ginger are mainly caused by [6]-gingerol and [6]-paradol and its homologues, which are the main constituents of pungent ginger principles (Lee and Surth, 1998; Keum et al., 2002). The mechanisms of the anti-tumor effects of gingerols and shogaols have not been fully clarified, but these compounds have shown a remarkable cytotoxicity and apoptosis-induction potential in human promyelocytic leukemia HL60 and leukemia K562 cell lines and in oral squamous carcinoma KB cell line, respectively (Lee and Surth, 1998; Keum et al., 2002; Leal et al., 2003). We did not find altered apoptotic indexes in the DMH-treated group submitted to dietary ginger. The increase of cell proliferation is an important condition for experimental and human colon carcinogenesis (Chang et al., 1997; Einspahr et al., 1997). Our results showed that DMH treatment enhanced cell proliferation in the colonic mucosa as demonstrated by the increased BrdU labeling indexes. Ginger meal did not change the proliferative indexes of the colonic crypts induced by DMH treatment. Therefore, the present results demonstrated a non-cytotoxic and non-chemopreventive effect of ginger on the colonic mucosa, as analyzed by the growth kinetics of the colon epithelium and by the ACF bioassay.

In this study ginger treatment per se did not induce any toxicity in the rats after a 10-week exposure period, as evidenced by unaltered body, relative liver and kidney weights; liver, kidney and colon morphology and serum biochemical analysis. These findings are of importance when implementing dietary measures for public health by increasing consumption of ginger, since it is a condiment and a widespread herbal medicine used for the treatment of many diseases. Experimentally, ginger treatment can reduce the total serum cholesterol by enhancement of the activity of the liver cholesterol-7 α-hydrolase or inhibition of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase, the bile-acid conversion and/or fecal excretion of cholesterol (Srinivasan and Sambaiah, 1991; Tanabe et al., 1993; Sharma et al., 1996). Our findings showed that ginger meal significantly reduced the serum levels of total cholesterol, corroborating the hypothesis of its hypocholesterolemic activity.

The present results indicate that ginger meal failed to inhibit the development of ACF in an experimental model of colon carcinogenesis induced by DMH in rats. Considering the beneficial effects of this spice in other in vitro and in vivo assay systems, especially its anti-inflammatory properties (Thomson et al., 2002; Surh, 2002; Penna et al., 2003; Young et al., 2005), the potential chemopreventive influence of ginger on the development of colon tumors should continue to be investigated.

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