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Coriandrum sativum — effect on lipid metabolism in 1,2-dimethyl hydrazine induced colon cancer

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Abstract

The biochemical effect of coriander seeds on lipid parameters in 1,2-dimethyl hydrazine (DMH) induced colon cancer in rats were studied. The study shows that the concentrations of cholesterol and cholesterol to phospholipid ratio decreased while the level of phospholipid increased significantly in the DMH control group compared to the spice administered group. Fecal dry weight, fecal neutral sterols and bile acids showed a sharp increase in the coriander-fed group compared with the DMH administered group. Thus, coriander plays a protective role against the deleterious effects in lipid metabolism in experimental colon cancer. © 2000 Published by Elsevier Science Ireland Ltd. All rights reserved.

Keywords: 1,2-Dimethyl hydrazine; Cholesterol; Phospholipid; Fecal neutral sterols; Bile acids

1. Introduction

Most spices are known to be a source of many vitamins and domestic remedy for many of the human disorders (Chopra et al., 1956; Nadkarni and Nadkarni, 1976). They exhibit a wide range of physiological and pharmacological effects (Beena et al., 1995). Environmental factors play a crucial role in the etiology of several types of cancer. Epidemiological and experimental studies suggest that dietary factors particularly saturated fatty acids play an important role in the development of cancer (Mekeown Eyssen et al., 1985; Graham et al., 1988; Sullivan et al., 1990). Spices are reported to possess carcinogenic (Chitra et al., 1994) and anticarcinogenic properties. The hypolipidemic properties of certain spices have been documented (Sharma et al., 1991; Ram et al., 1996). Available reports throw light on the fact that bile acids play a major part in promoting colon tumor both in animals and human subjects (Wilpart et al., 1983). Refter et al. (1983), Caderni et al. (1988) showed that bile acids induce neoplastic changes in both cultured colon mucosal cells and in the colon of the animal. In view of the daily intake of several spices and their beneficial effects on human beings, we have proposed to study the effect of coriander seeds, a commonly used spice in Indian cuisines on lipid metabolism in 1,2-dimethyl hydrazine (DMH) induced colon carcinogenesis using rats as experimental animals.

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2. Materials and methods

2.1. Plant material

Dried and powdered coriander seeds were used in the experiment.

2.2. Animals

Male albino rats of Sprague–Dawley strain weighing 60–70 g were used in the experiment. They were supplied with normal laboratory diet (Hindustan Lever Ltd.) and water was given ad libitum. They were divided into three groups of 12 rats each — group I, II and III. Group I served as normal group, group II as DMH control group and group III as experimental group.

2.3. Diet

Group I, normal laboratory diet; group II, normal laboratory diet + DMH injection; group III, normal laboratory diet + DMH injection + 10% powdered coriander seeds.

2.4. Induction of colon cancer

1,2-DMH was purchased from Sigma (St. Louis, MO). The duration of experiment was 30 weeks. The animals from groups II and III were given 1,2-DMH injection for 15 weeks. The animals received spice only during the period of carcinogen administration. Until the 30th week they were given normal laboratory diet.

2.5. Experiment

The rats were sacrificed at two time periods. An initial period was conducted 1 week after 15 consecutive weeks of injection (pre-neoplastic stage). The final sacrifice period was undertaken at the 30th week of the experiment (neoplastic stage). During the first 15 weeks of the experiment, feces were collected for 24 h, weighed, frozen at 20°C and later homogenized with equal weight of water and lyophilized to a fine powder.

2.6. Biochemical assays

The tissue lipids were extracted by the procedure of Folch et al. (1957) and used for various estimations. Total cholesterol (Abell et al., 1952) and phospholipid (Zilversmit and Davis, 1950) were estimated. Neutral sterols and bile acids were extracted (Grundy et al., 1965) and estimated (Snell et al., 1965). Statistical analysis by Bennet and Frankilin, 1967.

3. Results

At the end of the 15th week, the level of cholesterol increased in the liver, distal colon and intestine of the spice-fed group compared with the DMH control group. But at the end of 30th week, the concentration of cholesterol in the liver, intestine, proximal and distal colon showed a significant decrease in the experimental group compared with the DMH control group (Table 1). The concentration of phospholipids increased in the liver, intestine, proximal and distal colon of the experimental group compared with the control group (Table 2). But the ratio of cholesterol to phospholipid was lower in the spice-administered group compared with the DMH control group (Table 3). The fecal dry weight of the rat during the 15-week period is given in Fig. 1. Fecal sterols and fecal bile acids showed a sharp increase in the coriander-fed group compared with the DMH administered group (Figs. 2 and 3). The number of tumors detected in both DMH control and DMH spice group is shown in Fig. 4.

4. Discussion and conclusions

In our study an increase in the level of cholesterol was observed in the liver and intestine at the end of 15-week period (pre-neoplastic stage). This increase in the cholesterol levels in the early stage of colon carcinoma may be due to the increased synthesis of cholesterol in both the intestine and liver. Liver and intestine have been observed as important sites for cholesterol synthesis. Similar observations were reported earlier (Manoj, 1993).

But the level of cholesterol decreased in the coriander-fed group compared with the DMH control group at the end of the 30-week period. Cholesterol and their metabolites namely the secondary bile acids stimulate proliferative activity of colonic epithelium resulting in tumor promotion (Takano et al., 1981). The observed decrease in the level of cholesterol in experimental group may be due to lower cholesterogenesis (Petrovich et al., 1984) as well as increased excretion of sterols and their metabolites. The lower level of fecal sterols in DMH group than in normal might be ex-

Table 1
Effect of coriander seeds on the cholesterol levels of 1,2-DMH induced rats (mg/100 g)[a]

Tissue	15th Week			30th Week		
	Normal	DMH	DMH +coriander	Normal	DMH	DHM+coriander
Liver	396.01 ± 9.50	408.85 ± 9.81[N.S.]	420.57 ± 10.09[N.S.]	330 ± 11.55	490.32 ± 17.16**	431.13 ± 15.08*
Intestine	425 ± 11.90	436 ± 12.21[N.S.]	599.20 ± 16.78**	387.3 ± 11.23	564 ± 16.36**	444.78 ± 12.9**
Proximal colon	481.3 ± 15.40	382 ± 12.22	268.71 ± 8.6**	352 ± 10.91	420.6 ± 13.04**	349.43 ± 10.83**
Distal colon	585 ± 17.55	517.36 ± 15.52*	550 ± 16.50[N.S.]	420 ± 10.50	685 ± 17.12**	621.78 ± 15.54**

[a] Values of phospholipid are expressed as mean ± S.E.M.; normal group is compared with DMH control group; DMH group is compared with DMH+coriander group; student's t-test; **, $P<0.01$; *, $0.01<P<0.05$; N.S., not significant.

Table 2
Effect of coriander seeds on phospholipid levels of 1,2-DMH induced rats (mg/100 g)[a]

Tissue	15th Week			30th Week		
	Normal	DMH	DMH+coriander	Normal	DMH	DHM+coriander
Liver	228 ± 7.52	165 ± 5.45**	188 ± 6.20*	415 ± 9.96	360 ± 8.64**	450 ± 10.8**
Intestine	620 ± 12.40	450 ± 9**	497 ± 9.97*	680 ± 14.28	460 ± 9.66**	575 ± 12.08**
Proximal colon	480 ± 10.08	390 ± 9.75**	503 ± 12.58*	560 ± 12.32	410 ± 9.02**	540 ± 11.88**
Distal colon	810 ± 16.20	700 ± 14**	530 ± 10.60**	750 ± 15	560 ± 11.20**	640 ± 12.88**

[a] Values of phospholipid are expressed as mean ± S.E.M.; normal group is compared with DMH control group; DMH group is compared with DMH+coriander group; student's t-test, **, $P<0.01$; *, $0.01<P<0.05$.

Table 3
Effect of coriander seeds on cholesterol–phospholipid ratio in rats induced with 1,2-DMH[a]

Tissue	15th Week			30th Week		
	Normal	DMH	DMH+coriander	Normal	DMH	DHM+coriander
Liver	1.74 ± 0.063	2.48 ± 0.089**	2.24 ± 0.081[N.S.]	0.795 ± 0.03	1.362 ± 0.052*	0.958 ± 0.036*
Intestine	0.685 ± 0.026	0.969 ± 0.037**	1.206 ± 0.021**	0.570 ± 0.021	1.226 ± 0.04**	0.774 ± 0.028**
Proximal colon	1.003 ± 0.03	0.98 ± 0.036[N.S.]	0.534 ± 0.019**	0.629 ± 0.025	1.026 ± 0.044**	0.647 ± 0.025
Distal colon	0.722 ± 0.018	0.739 ± 0.029**	1.038 ± 0.04**	0.560 ± 0.021	1.233 ± 0.045**	0.972 ± 0.028**

[a] Values of cholesterol are expressed as mean ± S.E.M.; normal group is compared with DMH control group; DMH group is compared with DMH+coriander group; student's t-test, **, $P<0.01$; *, $0.01<P<0.05$; N.S., not significant.

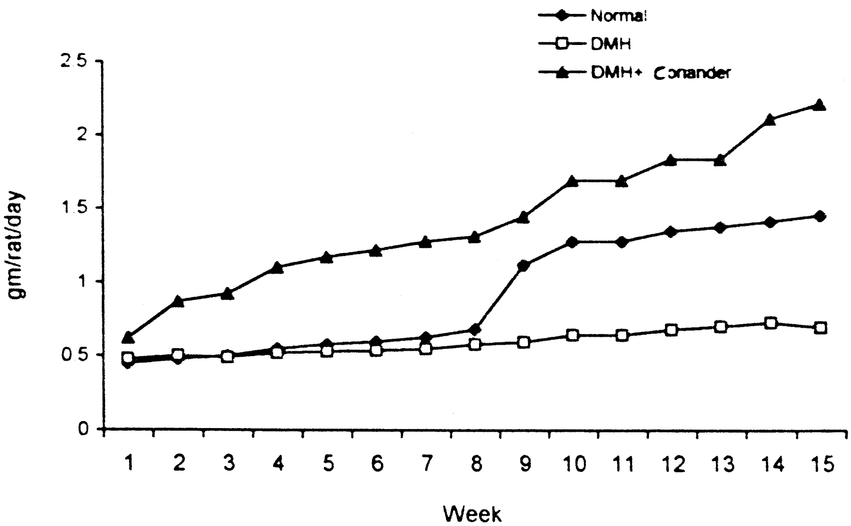

Fig. 1. Fecal dry weight of the rats during the first 15 weeks of the experiment.

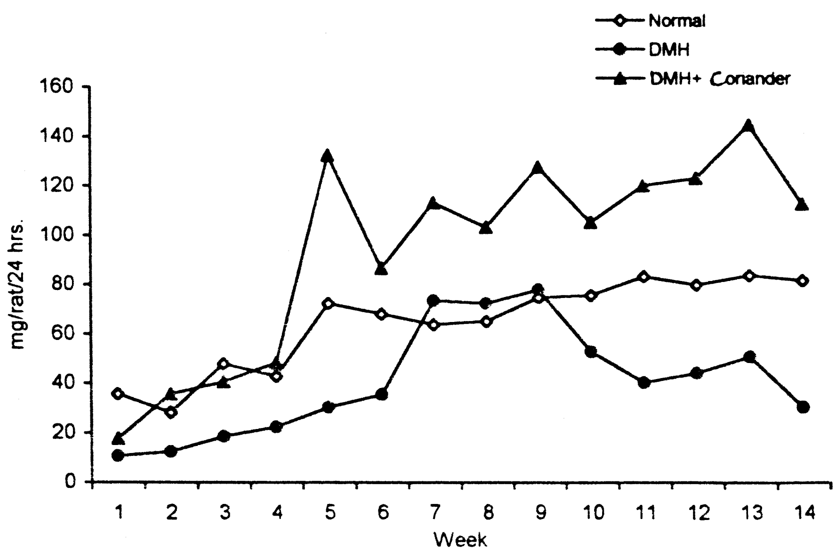

Fig. 2. Fecal neutral sterols of the rats during the first 15 weeks of the experiment.

plained by a very lower level of cholesterol in proximal and distal colon in comparison with normal group. This in turn may prevent the accumulation and metabolism of secondary bile acids by the colon microflora. The higher level of bile acids in the feces may be due to the absorption of less water-soluble bile acids by this spice. So, it can be assumed that coriander may reduce the absorption of bile acids in the ileum affecting the enterohepatic circulation of bile acids. Thus, enterohepatic pool is initially reduced and may be renewed by increased synthesis of bile acids from cholesterol thereby reducing the body cholesterol. The increased fecal excretion of bile acids and neutral sterols in the experimental group is in agreement with the increase in the activity of

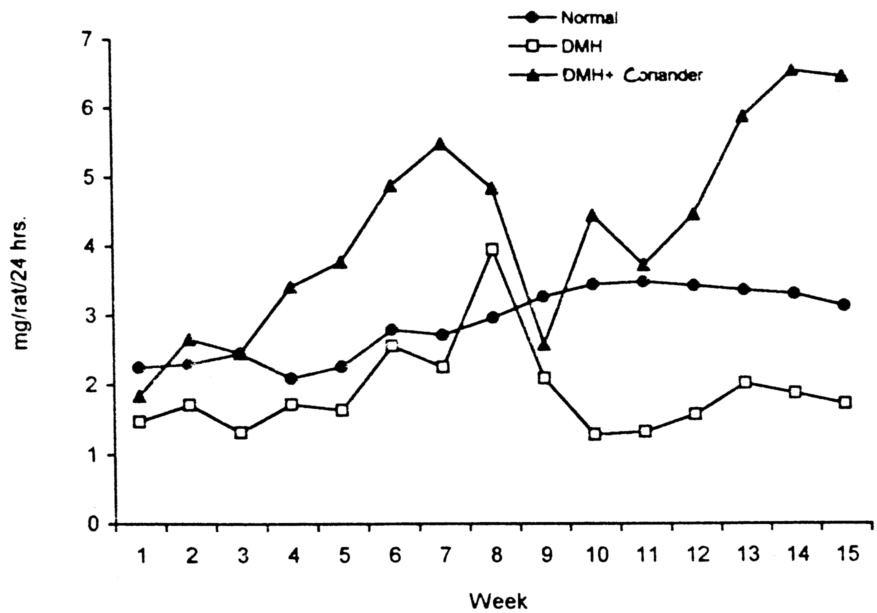

Fig. 3. Fecal bile acids of the rats during the first 15 weeks of the experiment.

hepatic cholesterol 7α-hydroxylase observed in rats administered with curcumin, capsaicin, ginger and mustard as reported by Srinivasan et al. (1991).

DMH-treated control rats showed decreased levels of phospholipids while the level of phospholipids increased significantly in the spice-fed group. Any alteration in the phospholipid metabolism will affect the properties and functions of membrane protein as phospholipids are vital components of biomembrane. The observed increase in the phospholipid content in the experimental group may be due to increased concentration of free fatty acids thereby decreasing the deleterious effects on the membrane leading to its dysfunction (Nalini et al., 1997).

The cholesterol–phospholipid ratio is closely related to membrane fluidity. The lower ratio of cholesterol to phospholipid in the spice-fed group is closely associated with membrane stability. Changes in the concentration of cholesterol will greatly affect the fluidity of the membrane and thereby can bring about abnormal changes in the membrane property and function (Marsch et al., 1976).

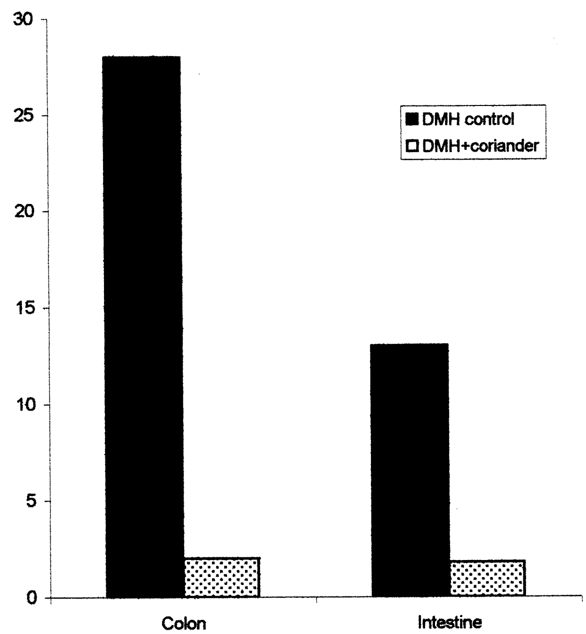

Fig. 4. Number of tumors detected in DMH control group and DMH + coriander group.

An elevated level of fecal dry weight observed in the experimental group is in agreement with previous reports (Chitra et al., 1994; Beena et al., 1996). This effect can be explained as one of the possible mechanisms by which coriander can inhibit colon tumorogenesis. The spice may have a higher water holding capacity and/or possess diluting and absorbing any carcinogens or promoters contained within the intestinal lumen.

Thus our study shows that in DMH-induced colon carcinoma in rats, there is increased concentration of lipids and also decreased excretion of bile acids in DMH control group compared to the experimental group. The administration of coriander counteracts this effect. The spice also prevents changes in the ratio of cholesterol to phospholipid thereby maintaining the membrane fluidity, integrity and function. Thus, the inclusion of this spice in the daily diet plays a significant role in the protection of colon against chemical carcinogenesis.

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