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Research Article
Chemoprotective Effect of Ginsenoside Against the 1,2-Dimethylhydrazine (DMH) Induced Colorectal Cancer in Rats

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Abstract

Background and Objective: Colorectal Cancer is the 2nd leading cause of cancer-related death among all types of cancers. Oxidative stress plays a crucial role in the expansion of colorectal cancer. Ginsenoside has a well known antioxidant agent and its proven antioxidant role against various diseases. This study analyzes the chemoprotective effect of ginsenoside against 1,2-dimethylhydrazine (DMH) induced colorectal cancer in rats. **Materials and Methods:** Swiss Wistar rats were used for colorectal cancer protocol. The rats were orally treated with ginsenoside. The body weight of the all-groups rats was estimated at regular time intervals. Tumour incidence, tumour weight and tumour volume were estimated. The antioxidant parameter, phase I and phase II enzymes were estimated in the hepatic and colorectal tissue. Pro-inflammatory cytokines, inflammatory mediators and proliferative parameters were estimated. **Results:** Ginsenoside treated rats significantly ($p<0.001$) boosted the body weight along with suppression of tumour weight, tumour incidence and tumour volume. Ginsenoside treated rats significantly ($p<0.001$) enhanced the level of glutathione (GSH), catalase (CAT), glutathione peroxidase (GPx), superoxide dismutase (SOD) and reduced the level of TBARS in the hepatic and colorectal tissue. Ginsenoside treated rats significantly ($p<0.001$) altered the level of lipid parameters. Ginsenoside treated rats significantly ($p<0.001$) suppressed the level of inflammatory cytokines, inflammatory mediators in the hepatic and colon tissue. **Conclusion:** Collectively, results suggest the antioxidant, anti-cell proliferative and anti-inflammatory effect of ginsenoside against DMH induced colorectal cancer.

Key words: Colorectal cancer, ginsenoside, inflammation, cell proliferation, antioxidant, glutathione peroxidase, cytokines

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Colorectal cancer has the highest cancer-related morbidity and mortality in developed countries[1,2]. Colorectal carcinogenesis is considered the 2nd leading cause of cancer-related death globally, behind cardiovascular disease[3]. The most common types of cancer are colorectal, lung and prostate cancer in men and colorectal, lung and breast cancer in women. According to studies, 880792 lives were died in 2018 (females 396,568 and males 484224), with 1.85 million new cases (823,303 females and 1.03 million males) estimated[4]. Cancer is divided into 3 stages, such as development, promotion and progression. The pathogenesis of colorectal cancer is very complex, but studies suggest that various factors, such as lifestyle, environment and diet. The regular colonic epithelium undergoes a malignant transition into the hyperproliferative epithelium, which leads to invasive and metastatic carcinogenesis[5-7]. The available treatment for colorectal cancer is chemotherapy and surgery which relies upon the position, stage and size of cancer. Treatment of cancer can start in any phase and is normally treated by subsequent surgery[2,7,8]. In various incidences, it starts earlier than surgical treatment in classifying the tumour size. Various investigations suggest that the number of colorectal cancer survivors has boosted in recent decades due to the expansion of medical procedures and chemotherapeutics[1,9]. But chemotherapy still has side effects such as diarrhoea, neutropenia, palmar-plantar erythrodysesthesia, thrombocytopenia and mucositis. A clinical study suggests that 20% of patients have adverse effects and around 1% of patients suffer from fatal toxicity[2,3,10]. Due to the limitations of chemotherapy, we still need a herbal based drug that has maximum effect with fewer side effects.

The 1,2-dimethylhydrazine (DMH) is a chemical agent commonly used for the induction of colorectal cancer in rodents. The DMH is subcutaneously administrated to the rodent and is metabolized in the liver tissue into methylazoxymethanol (MAM)[7-9]. The MAM (metabolite) undergo the colon tissue via blood or bile circulation to induce DNA mutations from G:C to A:T in genes involved in cell proliferation. Epithelial cells undergo pathogenesis after DMH treatment, progressing from minor lesion aberrant crypt foci (ACF) to malignant adenocarcinoma[11,12].

The cancer cell undergoes malignant transformation via various significant markers that directly or indirectly exhibit the way to suppress uncontrolled cell proliferation, cell death and boost the metastatic prospective and angiogenesis. Furthermore, recent research has revealed that inflammation plays a predictable role in carcinogenesis, which is both a cause and an effect of malignant conversion[10,13]. Genetically, the malignant conversion starts the appearance of an inflammatory reaction related to the mechanisms that direct the tumour expansion into the inflammatory milieu. Oxidative stress and free radical production activate a variety of transcription mediators, including Tumour Necrosis Factor-(TNF-α), AP-1 and Nuclear Factor kappa β (NF-κβ), causing normal cells to transform into tumour cells [7,14,15].

Furthermore, DMH has been demonstrated to induce the deposition of inducible iNOS and Cyclooxygenase-2 (COX-2) in the colon tissues. The COX-2 catalyzes the oxidative cyclization of arachidonic acid (AA) to prostaglandins PGH2 and PGG2 synthesize, whereas iNOS converts L-arginine into the citrulline and nitric oxide (NO)[16]. The iNOS and COX-2, both are pro-inflammatory molecules that are well known to be present in adenocarcinomas and preneoplastic colonic lesions. Furthermore, the reduction of inflammatory reactions is widely recognized as a new paradigm in colon cancer chemoprevention[16].

This method appears to be the most reliable for identifying colorectal cancer similar to human cancer. This method appears to be the most reliable for identifying colorectal cancer prevention strategies[7,10]. Interestingly, medicinal herb consumption is gaining worldwide attention because of its safety, effectiveness and bioavailability, especially in light of the vast range of side effects, low cure and high recurrence rates associated with conventional treatments[5,17].

In this experimental study, the authors estimated the chemoprotective effect of ginsenoside against the 1,2-dimethylhydrazine (DMH) induced colorectal cancer in rats and explore the underlying mechanism.

MATERIALS AND METHODS

Study area: The study was performed in the Department of General Surgery, Dezhou Municipal Hospital, Shandong 253012, China in 2021.

Chemicals: The DMH was purchased from the ACROS OrganicsTM (Thermo Fisher Scientific, USA). All the reagents were used in this experimental study was an analytical grade.

Animal: Swiss Wistar 50 rats (sex male, aged: 8-10 weeks, 150±20 g) were acquired from the institutional animal house. All the rodents were kept in the standard laboratory atmospheres (average humidity, temperature 22±5°C, 12 hrs dark/light cycles). The rats were received the water and regular pellet diet and standard diet mention in Table 1. All the research protocol was approved by the Institutional animal ethics committee.

Table 1: Ingredients of the diet

Ingredients	Normal diet	High fat diet
Wheat bran	26.7	22.3
Corn starch	28.5	24.3
Soybean flour	17.5	17.5
Fish meal	5.0	4.4
Bone meal	2.0	1.8
Yeast powder	1.0	0.9
Salt	1.0	0.9
Mineral mix	1.3	1.3
Vitamin mix	1.0	0.9
Lard	-	10.0
Cholesterol	-	3.0
Propylthiouracil	-	0.2
Sodium deoxycholate	-	0.5
Total	100.0	100.0

Table 2: List of experimental groups

Groups	Groups name	DMH treatment (mg kg^{-1})	Treatments
I	NC	-	1% Acacia
II	DMH	20	1% Acacia
III	DMH	20	GS (5 mg kg^{-1})
IV	DMH	20	GS (10 mg kg^{-1})
V	DMH	20	GS (15 mg kg^{-1})

NC: Normal control, DMH: 1,2-dimethylhydrazine, GS: Ginsenoside

DMH preparation: For the preparation of DMH, the DMH was dissolved in the EDTA (1 mM) and pH was adjusted to 6.5 (using the 1 mM of NaOH), for getting the strength of the carcinogen. The 20 mg kg^{-1} subcutaneous injection of DMH (20 mg kg^{-1} b.wt.) was used. The DMH administration was given to the rats continuous 4 weeks.

Test drug: Ginsenoside (GS) was used for testing the chemoprotective effect. Briefly, the test dose of GS was prepared via preparing the 1% suspension of acacia and the drug was suspended into the suspension.

Experimental protocol: The rats were grouped into 5 groups and each group contains 10 rats. The groups as presented in Table 2. The rats have received the oral administration of tested drugs and vehicles till 16 weeks. The body weight, food intake, water and urine output were estimated at a regular time interval.

At end of the experimental protocol, the rats were anaesthetized and blood samples were collected via puncturing the retro-orbital plexuses. The rats were sacrificed using the ketamine[4] and xylene and colon tissue was immediately removed, washed with the ice saline and preserved in the formalin (10%) and stored at -80°C for histopathological determination.

Antioxidant parameters: The previously reported method was used for the estimation of Thiobarbituric Acid Reactive Substance (TBARS), catalase (CAT), glutathione peroxidase (GPx), glutathione (GSH), superoxide dismutase (SOD) and glutathione reductase (GR) in the colon and liver tissue[1-3,8].

Phase I enzymes include cytochrome C, cytochrome b5 (Cyt-b5) and cytochrome P450 (CYP450) were estimated in the liver and colon tissue using the previously reported method with minor modification. Phase II enzymes such as and glutathione s-transferase (GST) and UDP-glucuronyl transferase were determined using the previously reported method with minor modification[4].

ELISA: The TNF-α, IL-1β and IL-6 were estimated using the ELISA kits following the manufacture protocol (Abnova, CA, USA).

The NOS and iNOS were estimated using the Assay kit using the manufacture protocol (Abnova, CA, USA) and COX-2 levels were determined using the ELISA kit following the manufacture protocol (Abcam, MA, USA).

Statistical observation: In this study, all the results were estimated as Mean±Standard Error Means (SEM). GraphPad Prism was used for the estimation of statistical analysis using the ANOVA (GraphPad Prism 8, San Diego, CA, USA). Tukey's test as a *post hoc* test was used for the determination of statistical analysis. The difference was estimated as statistically significant at $p<0.05$.

RESULTS

Tumour incidence and weight: No tumour incidence was observed in the untreated group rats. The DMH group rats exhibited an enhanced incidence of 100% tumour incidence and observed a tumour weight of 15.43±3.45 mm^3. The DMH rats treated with GS exhibited suppression of tumour incidence of 80, 66.87 and 22.34% at a dose level of 5, 10 and 15 mg kg^{-1}. The GS suppressed the tumour volume by 11.34±2.34, 6.42±1.73 and 0.29±0.37 at a dose-dependent manner (Table 3). The GS exhibited 26.52, 58.39 and 98.12% inhibition of tumour.

Body-weight: In this experimental study, we estimated the body weight at regular time intervals. The normal pattern increase in body weight was observed in the normal rats. DMH group showed an enhancement in body weight, but the enhancement in body weight did not follow a similar pattern to normal and tested drug group rats. The GS treated rats demonstrated the enhancement of body weight in a concentration-dependent manner (Table 4).

Lipid parameters: In colorectal cancer, alteration in the lipid parameters is a serious problem. In this study, DMH group rats demonstrated increased levels of TC, TG, LDL, VLDL and suppression of HDL levels. The GS treated group rats exhibited a reduction in the level of TC, TG, LDL, VLDL and enhancement in the level of HDL (Fig. 1).

Antioxidant parameters: It is well known that oxidative stress is boosted during colorectal cancer. The oxidative stress level was boosted in the colon and hepatic tissue. In this study, they estimated the antioxidant level in the hepatic and colorectal tissue. DMH group rats demonstrated a reduced level of GSH (Fig. 2a), GR (Fig. 2b), CAT (Fig. 2c), GPx (Fig. 2d) in the colon and hepatic tissue. The GS treatment significantly ($p<0.001$) boosted the level of GSH, GR, CAT, GPx in the colon and hepatic tissue.

Figure 2e exhibited the level of TBARS in the colon and hepatic tissue. The DMH group rats exhibited an augmented level of TBARS in the colon and hepatic tissue. Figure 2f demonstrated the SOD level in the colon and hepatic tissue. The DMH rats exhibited a reduction in the level of SOD in the colon and hepatic tissue and GS treatment significantly ($p<0.001$) boosted the level of SOD in the colon and hepatic tissue.

Table 3: Effect of GS on the total tumours, tumour incidence and tumour volume of all group rats

Groups	Total rats/No. of rats with tumours	Tumour incidence (%)	Tumour volume (mm^3)/rats	Inhibition (%)
NC	10/0	-	-	-
DMH	10/10	100.00	15.43±3.45	-
DMH+GS (5 mg kg^{-1})	10/8	80.00	11.34±2.34	26.52
DMH+GS (10 mg kg^{-1})	9/6	66.87	6.42±1.73	58.39
DMH+GS (15 mg kg^{-1})	9/2	22.34	0.29±0.37	98.12

Table 4: Effect of ginsenoside against 1,2-dimethylhydrazine (DMH) induced colorectal cancer in rats

	Weeks				
Groups	0	4	8	12	16
NC	151.34±5.46	168.3±6.12	189.3±5.83	206.2±5.42	228.3±4.93
DMH	158.34±6.43	162.2±7.53	169.3±5.43	172.2±4.89	177.3±5.09
DMH+GS (5 mg kg^{-1})	$159.3±5.43^{NS}$	$163.4±4.89^{NS}$	172.5±5.03*	176.3±6.06*	182.2±5.82**
DMH+GS (10 mg kg^{-1})	$157.8±4.89^{NS}$	171.0±5.04*	178.2±5.12*	182.3±4.82**	198.3±5.94***
DMH+GS (15 mg kg^{-1})	$151.4±5.44^{NS}$	165.0±4.78*	183.0±5.93**	198.3±5.05***	222.6±5.32***

*p<0.05, **p<0.01, ***p<0.001, #p<0.05 shows the difference between the DMH control and GS treated group rats, NC: Normal control, DMH: 1,2-dimethylhydrazine, GS: Ginsenoside and NS: Not significant

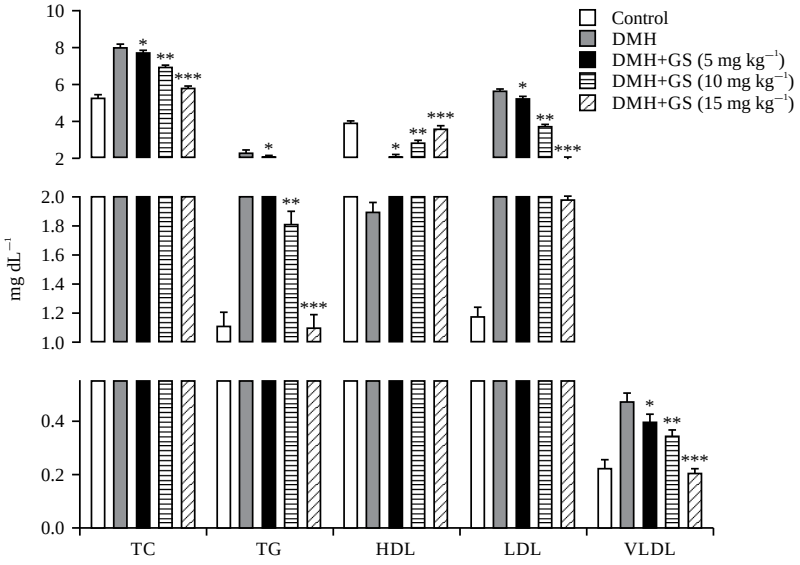

Fig. 1: Lipid parameters of a different group of rats

Date is presented as Mean±Standard deviation, one-way ANOVA followed by Tukey's *post hoc* test was performed for the statistical significance, where, *p<0.05, **p<0.01 and ***p<0.001 was considered as significant when compared with the DMH group rats

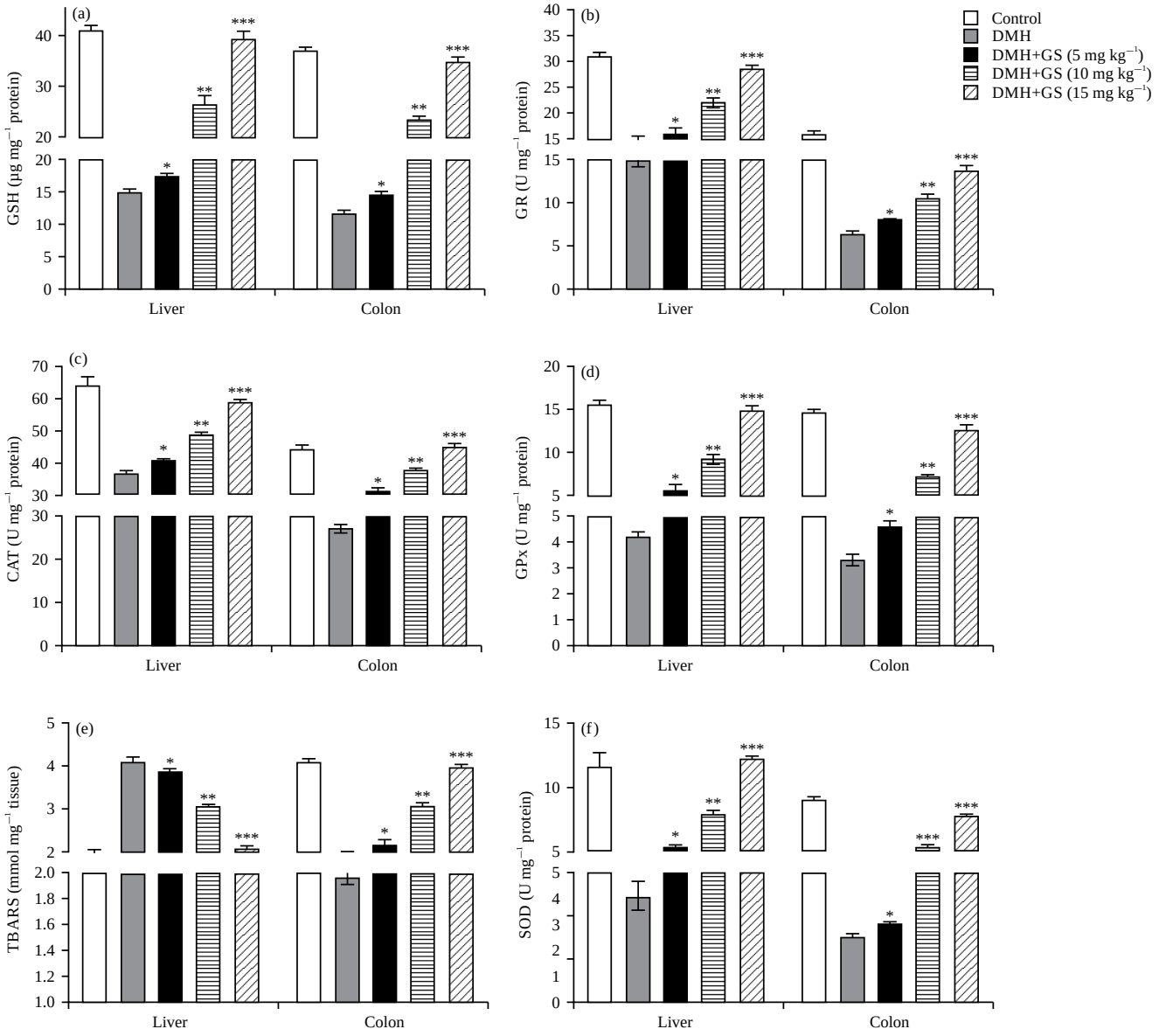

Fig. 2(a-f): Antioxidant parameters of a different group of rats, (a) GSH, (b) GR, (c) CAT, (d) GPx, (e) TBARS and (f) SOD

Data is presented as Mean±standard deviation. One-way ANOVA followed by Tukey's *post hoc* test was performed for the statistical significance, where, *p<0.05, **p<0.01 and ***p<0.001 was considered as significant when compared with the DMH group rats

Phase I and II enzymes: Figure 3 demonstrated the effect of GS and DMH on the phase I and phase II enzymes. The DMH group rats showed a boosted level of cytochrome P_{450} (Fig. 3a) and cytochrome B_5 (Fig. 3b) and GS treated group rats significantly (p<0.001) suppressed the level of cytochrome P_{450} and cytochrome B_5.

The GST (Fig. 3c) and UDP-GT (Fig. 3d) levels were significantly (p<0.001) suppressed after DHM treatment, whereas, GS treated rats significantly (p<0.001) booted the level of GST and UDP-GT in the colon and hepatic tissue.

Cytochrome P_{450} and cytochrome B_5

Inflammatory cytokines: In colorectal cancer, the inflammatory reaction is boosted due to the expansion of cancerous cells. The TNF-(Fig. 4a), IL-1 (Fig. 4b) and IL-6 (Fig. 4c) levels were higher in the DMH group rats' colon and hepatic tissue. The GS treatment significantly (p<0.001) suppressed the level of inflammatory cytokines in the colon and hepatic tissue.

MPO: The DMH group rats exhibited an increased level of MPO in the colon and hepatic tissue. The GS

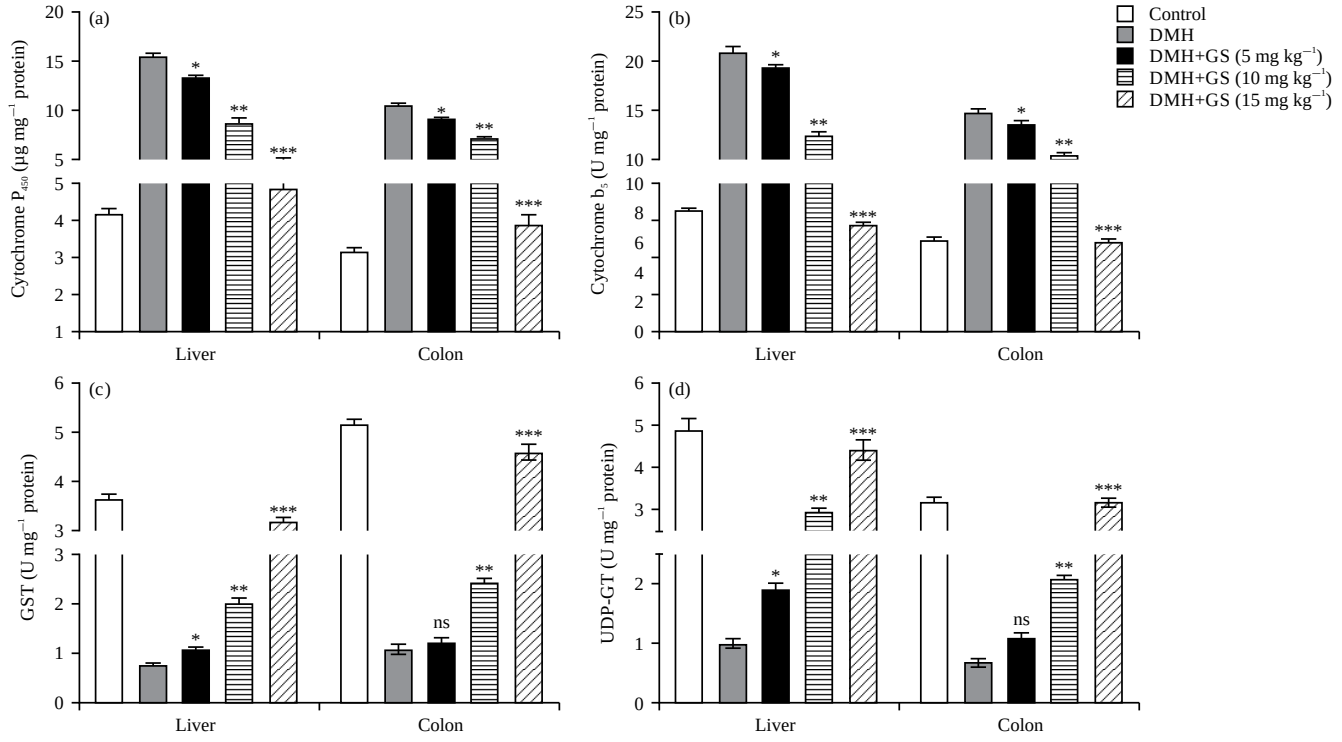

Fig. 3(a-d): Phase I and II enzyme parameters of a different group of rats, (a) Cytochrome P_{450}, (b) Cytochrome b_5, (c) GST and (d) UDP-GT

Data is presented as Mean±Standard deviation, one-way ANOVA followed by Tukey's *post hoc* test was performed for the statistical significance, where, *p<0.05, **p<0.01 and ***p<0.001 was considered as significant when compared with the DMH group rats, ns: Not significant

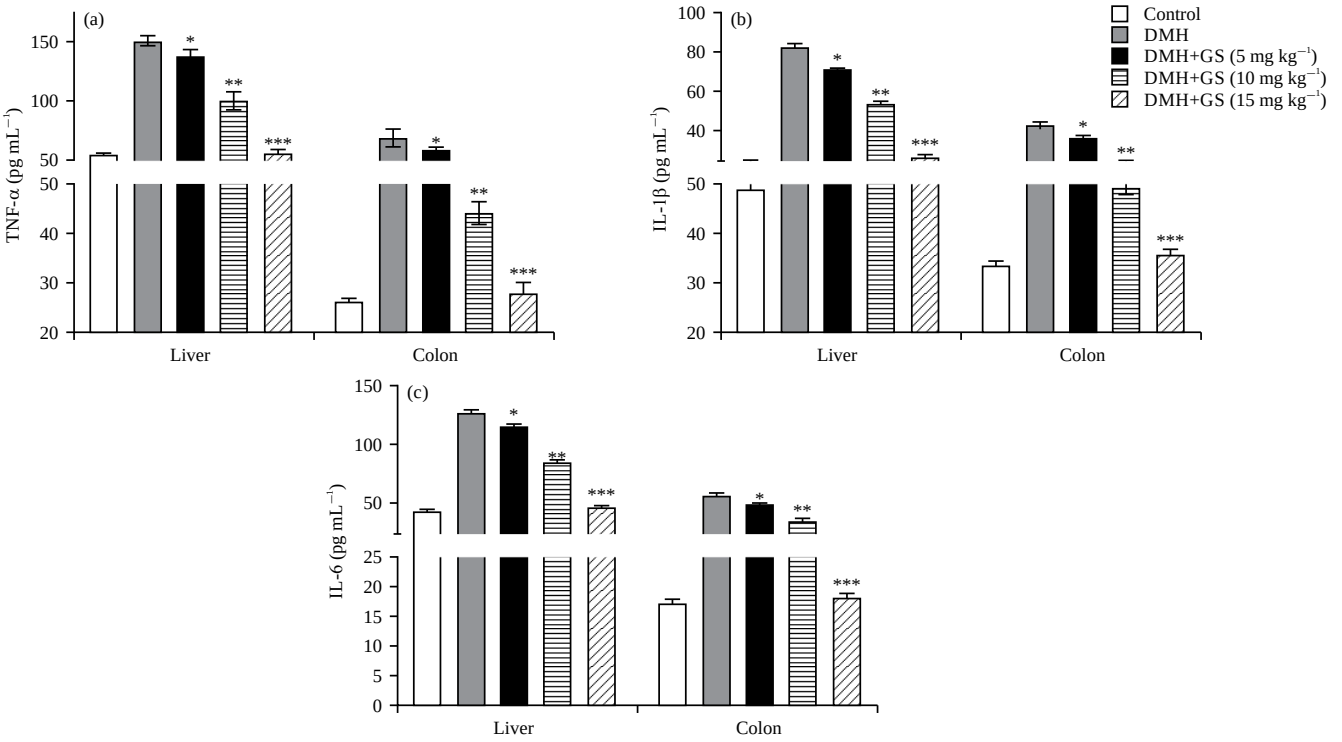

Fig. 4(a-c): Inflammatory cytokines parameters of a different group of rats, (a) TNF-α, (b) IL-1β and (c) IL-6

Data is presented as Mean±Standard deviation, one-way ANOVA followed by Tukey's *post hoc* test was performed for the statistical significance, where, *p<0.05, **p<0.01 and ***p<0.001 was considered as significant when compared with the DMH group rats

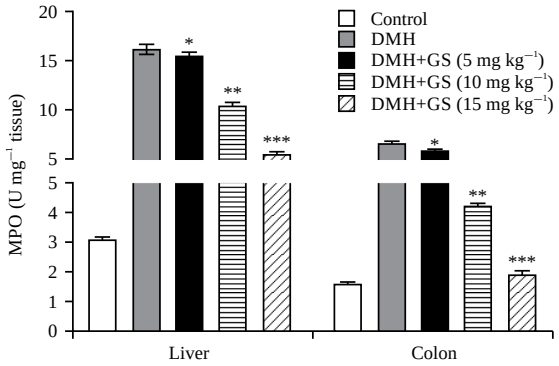

Fig. 5: MPO level of a different group of rats

Date is presented as Mean±Standard deviation, one-way ANOVA followed by Tukey's *post hoc* test was performed for the statistical significance, where, *p<0.05, **p<0.01 and ***p<0.001 was considered as significant when compared with the DMH group rats

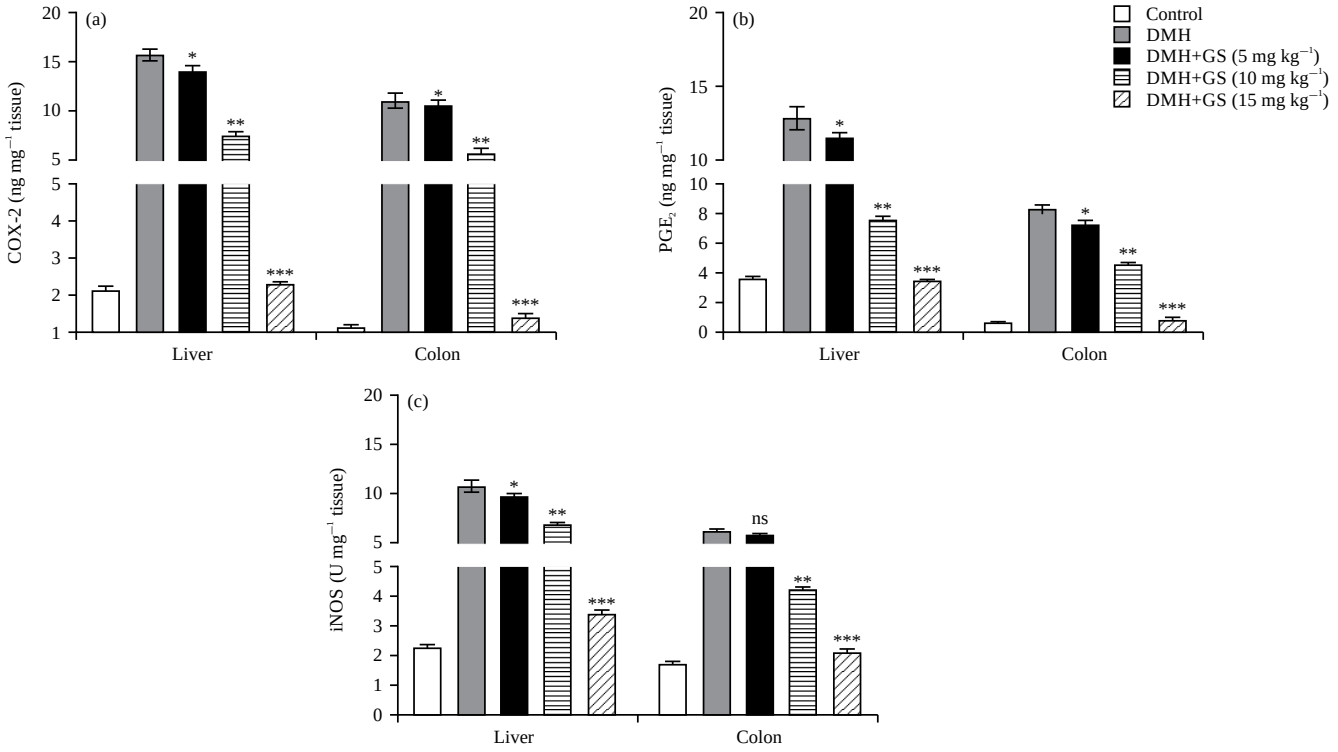

Fig. 6(a-c): Inflammatory parameters of a different group of rats, (a) COX-2, (b) PGE_2 and (c) iNOS

Data is presented as Mean±Standard deviation, one-way ANOVA followed by Tukey's *post hoc* test was performed for the statistical significance, where, *p<0.05, **p<0.01 and ***p<0.001 was considered as significant when compared with the DMH group rats, ns: Not significant

treatment significantly (p<0.001) suppressed the level of MPO in the colon and hepatic tissue (Fig. 5).

Inflammatory mediators: Inflammation plays an important role in the expansion of colorectal cancer disease. The DMH group rats exhibited increased levels of COX-2 (Fig. 6a), PGE_2 (Fig. 6b) and iNOS (Fig. 6c) in the colon and hepatic tissue. DMH rats treated with the GS significantly (p<0.001) suppressed the level of inflammatory parameters in the colon and hepatic tissue.

DISCUSSION

In this study, DMH treated rats exhibited an in increase tumour incidence, tumour volume and GS treatment significantly suppressed the tumour incidence and volume. DHM treated rats exhibited the suppression of body weight and GS treatment considerably increased the body weight. The GS treatment significantly (p<0.001) reduced the level of TG, TC, LDL, VLDL and boosted the level of HDL in DMH induced colorectal cancer rats. The GS received rats altered

the level of antioxidants, inflammatory cytokines, an inflammatory mediator in the colon and hepatic tissue. Chemotherapeutics are the best approach among all types of available treatments for cancer and isolated Phyto-constituents and herbal medicine have the potential benefit over conventional treatments with more protective effects with one or fewer side effects[18-20]. According to previous research, plant-based medicine and Phyto-constituents are nontoxic products and are usually observed in different dietary vegetables and fruits[21-23]. Previous research indicates that various plant-based phytoconstituents have been used to treat as chemopreventive agents against various types of cancers[24,25]. Colorectal cancer is regularly detected and pathophysiological results suggest that continuous oxidative stress, boosted the incidence of colorectal cancer[25,26]. Ginsenoside is a well-known antioxidant and it shows free radical scavenging activity against various diseases[27-30]. In this experimental study, we tried to analyze the chemoprotective effect of ginsenoside against DMH induced colorectal cancer.

After the DHM treatment, the body weight of rats was commonly reduced due to the expansion of colorectal cancer[1,9]. The body weight of DMH rats was reduced due to boosting the tumour volume and tumour incidence by enhancing the polyps driven anorexia and cachexia[4]. Ginsenoside treated rats exhibited an improvement in body weight due to metabolic modification induced by the DMH and the ginsenoside treatment restored the cellular metabolic impairment.

The DMH is a well-known colorectal carcinogen that directly stimulates the production/generation of reactive oxygen species (ROS) in colorectal cells, stabilising their metabolism and ultimately inducing colorectal cancer, as evidenced by numerous tumour markers variations[4]. After inducing colorectal cancer with DMH, the cellular metabolism is activated, resulting in increased production of free radicals and, ultimately, oxidative stress[2,14,31]. The increased level of ROS in the cells induces the worsening of the endogenous antioxidant and boosts the production of free radicals which starts the deterioration of tissue[11,12]. Previous research suggests that ROS induced oxidative stress is commonly observed in both fibrosis and malignancy, leading to cancer-related fibroblasts[4]. For the treatment of cancer, the researchers targeted oxidative stress to suppress the cancer disease.

It is well proven that oxidative stress boosts cancer incidence and many researchers use the potent antioxidant to treat cancer disease[1,8]. Previous reports suggest that lipid peroxidation (LPO) is involved in the fundamental function of tumorigenesis and may lead to generating/producing various toxic substances, including TBARS and malonaldehyde (MDA)[4,32]. These toxic substances can damage cellular products viz., DNA thereby signifying tumourigenicity and mutagenicity[2,31]. After administration of DMH, the level of LPO such as TBARS in the colon and hepatic tissue was boosted. The rats that received the ginsenoside reduced the level of TBARS (LPO mediators). Ginsenoside exhibited anti-lipid peroxidative properties against DMH induced colorectal cancer, which was possible due to its potent antioxidant agents[33,34]. Antioxidants are well known for their ability to catalyse disproportionate reactions of their substrate-free radicals that are spontaneously formed by *in vivo* cytochrome P450 metabolism, inflammatory processes and oxidative phosphorylation, among other things[4]. The DMH induced colorectal rats demonstrated the suppressed level of GSH, SOD, GPx and CAT, which showed the complete disruption of the endogenous antioxidant dependent mechanism of colorectal cancer. The suppression of endogenous antioxidant enzymes might be due to suppression of consumption or formation of antioxidant levels and boost the generation of free radicals[4,35,36]. Ginsenoside treatment considerably augmented the level of endogenous antioxidant enzymes in the liver and colorectal tissue. The antioxidant effect of ginsenoside is due to its capability to reduce LPO, simultaneously its free radical scavenging potential. Few investigations support our finding that antioxidant therapy treats colorectal cancer[2,31,37]. Ginsenoside could also successfully suppress the production of free radicals and enhance the level of endogenous antioxidants. It is well proved that endogenous antioxidant enzymes play an important role to eradicate free radicals. During the cancer condition, free radical production is increased due to the expansion of cancerous cells and suppression of endogenous antioxidants[10,34]. A similar momentum was observed in the DMH induced colorectal cancer group rats. The DMH is a potent carcinogen that can metabolize in hepatic tissue and initiate free radical production. The SOD is the 1st line endogenous antioxidant that protects the cells from the attack of free radicals. The SOD catalyze the superoxide and hydrogen peroxide with the help of GPx and formed the water[38,39]. The CAT is the other 1st line antioxidant that protects the cells from free radicals. The CAT maintained a balance between the destruction and production of ROS in the tissue.

The cytochrome P450 enzymes stimulate the metabolism of DMH, resulting in inactive metabolites that are essential for tumour growth[4]. The reactive products of DMH are removed from the body through phase II enzymes including GR and GST. The DMH group rats exhibited a reduced level of GR and GST and boosted levels of Cytb5 and P450, which suggest the expansion or progression of colorectal cancer in the rodents[16]. The same result was observed in the previous research. The data anticipate that ginsenoside plays a dual role through suppression of phase I enzymes and enhancement of the activity of phase II enzymes, accordingly supporting detoxification and excretion of free radicals after DHM administration[4,16]. Epidemiologic studies have been increasingly supporting the idea that there is a strong link between inflammatory disorders and the potential for cancer growth. Previous research suggests that the various molecules play a direct or indirect role in the generation of proliferation and inflammation during carcinogenesis[15,38,40]. The COX-2, an inducible prostaglandin-endoperoxide synthase 2 has been related to tumour inflammation and cell proliferation. Previous research suggests that inflammatory reactions boost cytokines, growth factors and boost the tumour. The TNF-α is a cell signalling agent that is released when macrophages are activated and it regulates the immune response, inflammation and tumour cell necrosis[41,42]. The IL-6 cytokine is controlled by the NF-κB and play an important role in the activation of the tumour via activation of multiplication of tumour instigating cells. The iNOS and IL-1β are the inflammatory cytokine mediators and these play a crucial role in boosting the tumour propagation and forcefulness of cancer cells[4]. Previous research suggests that the inflammatory cytokines, inflammatory mediators and proliferative markers play a crucial role in the progression of colorectal cancer[15,38,42,43]. The DMH induced colorectal group rats exhibited a similar effect and ginsenoside treatment significantly suppressed the levels of inflammatory cytokines, inflammatory mediators and proliferation parameters.

CONCLUSION

In this experimental study, we have observed that ginsenoside suppressed the tumour incidence and tumour volume and increased the body weight. Ginsenoside reduced the endogenous antioxidant, phase I and phase II enzymes. Ginsenoside treatment considerably suppressed the inflammatory cytokines, inflammatory mediators and proliferative parameters. Based on these results, ginsenoside is a potent drug against colorectal cancer via an antioxidant and anti-inflammatory mechanism.

SIGNIFICANCE STATEMENT

This study discovers the chemoprotective effect of ginsenoside against DMH induced colorectal cancer that can be beneficial for colorectal cancer. This study will help the researcher to uncover the critical area of colorectal cancer that many researchers were not able to explore. Thus, a new therapy on colorectal cancer may be arrived at.

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