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Prevention and therapy of 1,2-dimethyl hydrazine induced colon carcinogenesis by Ferula assa-foetida hydroalcoholic extract

Abstract: Objective: In this study, we have evaluated the chemopreventive and chemotherapeutic effects of Ferula assa-foetida hydroalcoholic extract in 1,2-dimethyl hydrazine (DMH) induced colon carcinogenesis.

Methods: Male Wistar rats were divided into 6 groups: a negative control group without DMH; control group with injected DMH (20 mg/Kg b.w) and four groups receiving DMH + F. assa-foetida extract (6.25 and 12.5 mg/Kg b.w) as chemopreventive and chemotherapeutic groups. The effects of the extracts were assessed by estimating the hepatic oxidative stress/antioxidant parameters such as malondialdehyde, glutathione and ferric reducing ability of plasma (MDA, GSH, FRAP) and the detoxification enzymes; glutathione S-transferase and Cytochrome P450 (GST and CYP450). Moreover, the colonic β-catenin protein was examined in colon tissues followed by the histopathological analysis.

Results: The results showed that the F. assa-foetida extract markedly reversed the increased levels of CYP450, FRAP and β-catenin and also modulated the reduction of GST (activities and protein) and GSH levels. Histological observations of liver tissue correlated with the above biochemical findings indicating the decrease in the aberrant crypt foci (ACF) formations in the extract treated groups.

Conclusion: The achieved results suggested the beneficial effect of the extracts on DMH metabolic processes in the colon indicating its chemopreventive and chemotherapeutic effects on colon carcinogenesis induced by DMH.

Keywords: Antioxidants, DMH, Colon tumor, Ferula assa-foetida, Oxidative stress, Xenobiotic Metabolizing enzymes

Özet: Amaç: Bu çalışmada Ferula assa-foetida hidroalkolik ekstraktının, 1, 2-dimetil hidrazin (DMH) ile indüklenmiş kolon kanserindeki kemopreventif ve kemoterapötik etkileri değerlendirilmiştir.

Metod: Erkek Wistar sıçanları 6 gruba bölünerek çalışılmıştır. Bunlardan negatif kontrol grubuna DMH verilmemiştir Kontrol grubuna ise DMH (20mg/Kg v.a.) enjekte edilmiştir. Kalan 4 gruba ise DMH + F. assa-foetida ekstraktı kemopreventif ve kemoterapötik olarak (6.25 ve 12.5 mg/Kg v.a.) verilmiştir. Ekstrakt etkilerinin ölçülmüş için hepatik oksidatif stres/antioksidan parametreleri, malondialdehit (MDA), glutatyon (GSH), ve plazmada demir indirgeme kapasitesi (FRAP) ile detoksifikasyon

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enzimlerinden glutatyon S transferaz (GST) ve Sitokrom P<sub>450</sub> (CYP<sub>450</sub>) saptanmıştır. Ayrıca histopatolojik analizlerden sonra kalın bağışıklık dokusunda kalın bağışıklık β-ka-tenin proteinine de incelememiştir.

Bulgular: Elde edilen sonuçlara göre F. assa-foetida ek-traktları yükselmış CYP<sub>450</sub>, FRAP ve β-katenin düzeylerini önemli derecede tersine çevirmiş ve ayrıca GST (aktivitesini ve proteinini) ve GSH düzeylerinin indirgenmesini ayarlamıştır. Ekstrakt uygulanan gruplarda, karaciğer dokusunun histolojik analizleri de yukarıdaki sonuçları uyumlu olarak anormal kript odakların oluşumunda azalma göstermiştir. Ekstrakt uygulanan gruplarda, karaciğer dokusunun histolojik analizleri de yukarıdaki sonuçları uyumlu olarak anormal kript odakların oluşumunda azalma göstermiştir.

Sonuç: Elde edilen bulgular ekstraktların, DMH ile indük-lenmiş kalın bağışıklık kanserlerinde kemopreventif ve kemoterapötik etkileri olduğunu, kalın bağırsaktaki DMH metabolizma süreçleri üzerindeki faydali etkileri ile göstermiştir.

Anahtar Kelimeler: Antioksidanlar, DMH, Kalın bağışıklık tümörleri, Ferula assa-foetida, Oksidatift stres, Ksenobiyo- tik metabolik enzimler

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Introduction

Colorectal cancer with age-adjusted rate of 6–79 per 100,000 people per year is the fourth most common cancer in Iran [1]. Also, globally more than 1 million people get colorectal cancer every year [2] resulting in about 715,000 deaths as of 2010 up from 490,000 in 1990 [3]. Since 2012, it is the second most common cause of cancer in women (9.2% of diagnoses) and the third most common in men (10.0%) [4] and also the fourth most common cause of cancer death after lung, stomach, and liver cancer. After genetic risk factors, other risk factors include nutrition, older age, male gender, high intake of fat, alcohol or red meat, obesity, smoking, and a lack of physical exercise [5].

The active metabolites of most carcinogens are thought to evoke the formation of oxygen-derived free radicals and intermediates of oxygen products such as hydrogen peroxides. Colon cancer is frequently a patho-logical consequence of persistent oxidative stress and inflammation [6,7]. 1, 2-Dimethylhydrazine (DMH) is a powerful colon specific carcinogen and it is being widely used to induce colon cancer in rodents [8,9]. The cells at the subcutaneous site do not possess enzymes capable of reacting with DMH. Hence, subcutaneously injected DMH reaches the liver via circulation, and gets metabolized into various intermediates such as azoxymethane (AOM) and methylazoxymethanol (MAM) [10,11]. Later on MAM is transported to the colon via bile or blood to generate its ultimate carcinogenic metabolite, electrophilic methyldi-azonium ion, which in turn generates carbonium ion that is responsible for the methylation of nucleic acids that triggers colon carcinogenesis [10,12,13].

Current dietary recommendations to prevent colorec-tal cancer include increasing the consumption of whole grains, fruits and vegetables. The evidence for fiber and fruits and vegetables however is poor [14]. Recently, there has been growing interest in natural antioxidants as safer and fewer side effects exert anticarcinogenic action by modulating the oxidative/antioxidant status in the tissues [15,16].

Ferula assa-foetida (Asafoetida, Stinking assa) grows in Iran, Afghanistan and Kashmir called “Anghouzeh“,“Khorakoma” and “Anguzakoma” in Iran which belongs to the Apiaceae family. It is herbaceous and perennial and grows up to 2 m high [17]. Asafoetida has been used as a spice and a folk phyto medicine for cen-turies. Asafoetida has a characteristic sulfurous odor and a bitter taste. It is used as a flavoring spice in a variety of foods, particularly in India. In addition, Nepali people regularly consume it in their daily diets, and it is believed that asafetida has aphrodisiac, sedative and diuretic prop-erties [18]. In addition, it is not only used as a culinary spice but also traditionally used to treat various diseas-es, including antispasmodic [19], aromatic, carminative, digestive, expectorant, laxative [20], sedative, nerve, analgesic, anthelmintic, antifungal [21–23], anti-diabetic [24], anti-inflammatory, anti-mutagenic, aphrodisiac and antiseptic properties [25]. Asafoetida consists of three main fractions, including resin (40–64%), gum (25%) and essential oils (10–17%) [26]. The resin fraction contains ferulic acid and its esters, coumariins, sesquieterpenic cou-marins and other terpenoids. The gum includes glucose, galactose, l-arabinose, rhamnose, glucuronic acid, poly-saccharides and glycoproteins, and the volatile fraction contains sulfur-containing compounds, monoterpenes and other volatile terpenoids [27].

Despite these reports, however, no previous inves-tigations have been made to examine the chemopreventive and chemotherapeutic activities of F. assa-foetida hydroalcoholic extract in experimental animal model against DMH induce colon carcinogenesis. Therefore, the present study has focused on the mechanism or the ways of the chemopreventive and chemotherapeutic effects of F. assa-foetida hydroalcoholic extracts -cultivated in Iran-
in colon carcinogenesis induced by DMH in vivo system regarding parameters related to oxidative stress and xenobiotic metabolizing enzymes in liver and plasma of rats accompany with histopathological examinations.

**Material and Methods**

The graphical protocol of the methods is shown in Figure 1. Male *Wistar* rats were used throughout this study. The

**Plant preparation**

*Ferula assa-foetida* hydroalcoholic extract cultured in Iran were purchased from Barij Essence Pharmaceutical Company, Kashan, Iran.

**Induction of colon tumor in rats**

Male *Wistar* rats were used throughout this study. The
animals were obtained from the Pasteur Institute of Iran and maintained in the animal house facilities. Animal studies were approved by the Medical Ethics Committee of Tarbiat Modares University. This Ethics Committee was based on the World Medical Association Declaration of Helsinki (adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964). Adult animals were 3–4 months of age, weighing 150±20 g. They were maintained on a commercial pellet food and tap water ad libitum. DMH was dissolved in 1 mM EDTA just before use and the pH was adjusted to 6.5 with 1 mM NaOH to ensure the stability of the chemical. The animals were divided into 6 groups (n=10). The rats in group 1 (negative control group) received (0.3 ml) of EDTA s.c injection- the vehicle of DMH once a week for 18 weeks. Rats in group 2 received DMH dissolved in EDTA (20 mg/kg b.w) injection (s.c) once a week for 18 weeks. Rats in group 3 and 4 were given s.c injections of DMH (20 mg/kg b.w) for 18 weeks and i.p injections of F. assa-foetida hydro alcoholic extract (6.25, 12.5 mg/Kg b.w doses) together daily for 4 months and considered as chemopreventive groups. Rats in group 5 and 6 were given DMH injections (20 mg/kg b.w) for 18 weeks and 4 months afterward, F. assa-foetida hydroalcoholic extracts (6.25, 12.5 mg/Kg b.w) were injected i.p until 8 months and considered as chemotherapeutic groups.

Colon tumor enumeration

At the end of the experiment (8 months), the animals were anesthetized and the blood was collected by heart puncture. Then, the animals were scarified, liver tissues were removed and stored in a freezer (−80 °C). Also, their colon tissues were removed and divided into 3 sections, and designated as section a – proximal colon, section b – middle colon, and section c – distal colon. processed for histological and biochemical assays.

Biochemical assays

Glutathione (GSH) estimation

GSH was estimated in liver homogenate based on the protocol of the purchased kit from BioVision, Inc., USA.

Ferric reducing ability of plasma (FRAP) assay

This assay was performed using TPTZ reagent as described by Benzie and Strain (1996). FRAP level was calculated by plotting a standard curve of absorbance against μmol/L concentration of Fe (II) standard solution.

Malondialdehyde (MDA) assay

A weighed portion of the liver was homogenized in phosphate buffer (100 mM, pH 7.0) and used to measure the concentration of thiobarbituric acid reacting substances (TBARS) as an indicator of lipid peroxidation. The concentration of TBARS was measured spectrophotometrically according to the instruction of the kit purchased from Enzo Life Sciences, Inc., UK.

Glutathione S-transferase (GST) activity

Liver cytosolic GST activities were measured spectrophotometrically using CDNB as substrate as described by Habig et al. (1974). The specific activity was calculated based on the nmol/min/mg protein in samples which was measured by Bradford assay [28].

GST protein assay

Liver cytosolic GST protein level was measured by ELISA as described in the instruction of the kit buying from Bioassay Technology Laboratory, China.

Cytochrome P450 (CYP450) activity

CYP450 protein level was performed by ELISA on liver preparations according to the procedure described in the kit from Bioassay Technology Laboratory, China.

Measurement of β-catenin at protein levels

β-Catenin levels in colonic preparations were measured quantitatively using a commercially available kit (Bioassay Technology Laboratory, China). The assay was performed according to the manufacturer’s instructions.

Pathological observation of aberrant crypts (AC) and aberrant crypt foci (ACF) formations

The pathological analysis of AC and ACF formations was described [29,30]. Briefly, after a total experimental period
of 8 months, the animals were sacrificed and the colons were removed, cut open along the longitudinal axis from cecum to anus and were flushed with PBS solution. The colons were assessed for the macroscopic changes. The total number of the ACF in the distal one third and the proximal two thirds of colon for each rat was determined in 2 (1-1.2 cm²) and 4 cm sections of the colon starting from the distal to the proximal end of the colons. The specimens were sandwiched between filter papers, fixed in 10% neutral buffered formalin and stained with 0.2% methylene blue in saline for 2-3 minutes and then placed mucosal slides up on a microscopic slide [31]. In this study, ACFs were easily identified under the light microscopy at 40* magnification, by their large and prominent luminal opening. Total number of ACF and the number of ACF with four or more ACs were counted separately in the distal one third and the proximal two thirds of colon for each rat. Aberrant crypts were distinguished from the surrounding normal crypts by their increased size, slit-like opening, thick and darker stained epithelia and pericryptal zone. For assessment of malignancy of the induced lesion, the number of ACF with four or more ACs as malignancy index was counted.

Statistical analysis

Data are presented as means±Standard error of mean (SEM). The results were subjected to One-way ANOVA followed by Tukey’s HSD using SPSS (version 19.0) software. Significant levels were defined as P<0.05.

Results

The effects of Ferula assa-foetida hydroalcoholic extract on hepatic oxidative injury parameters in colon cancer induced by DMH

DMH treatment showed a considerable (P<0.05) decrease in GSH level (Fig. 2). The experimental rats treated with both doses of Ferula assa-foetida extracts as chemopreventive and chemotherapeutic groups showed significant (P<0.05) elevation in GSH levels as compared to DMH-treated rats (Fig. 2). Administration of DMH to rats for 18 weeks led to a significant increase (P<0.05) in liver FRAP level as compared to the control rats (Fig. 3). Although, the chemopreventive and chemotherapeutic groups that treated with F. assa-foetida at both experimental doses could remarkably (P<0.05) returned the level of the FRAP to the normal value (Fig. 3). Although there were no signi-
significant changes (P>0.05) observed in MDA levels in *F. assa-foetida* extract treated rats when compared to the control group (Fig. 4).

**Effects of *Ferula assa-foetida* hydroalcoholic extract on the activities of hepatic detoxification enzymes (GST and CYP*<sub>450</sub>*)**

The CYP<sub>450</sub> activity in the liver of experimental rats injected with DMH increased considerably (P<0.05) in relation to the control group (Fig. 5). The administration of *F. assa-foetida* extracts in chemopreventive and chemotherapeutic groups could significantly decrease the hepatic CYP<sub>450</sub> at both doses (Fig. 5). In addition, a significant reduction in serums GST activity (Fig. 6) and protein (Fig. 7) was observed in DMH groups when compared to the normal group. Treatment of chemopreventive and chemotherapeutic groups with the *F. assa-foetida* extracts caused a significantly (P<0.05) increased in the level of GST activity and also protein level (except for group 3) (Figs. 6, 7).

**The effects of *Ferula assa-foetida* hydroalcoholic extract on colonic β-catenin protein level in colon cancer induced by DMH**

As shown in Figure 8, the levels of β-catenin in colonic tissues of DMH-treated rats were significantly (P<0.05) increased. While, the administration of *F. assa-foetida* extract in chemopreventive and chemotherapeutic groups produced a surprisingly (P<0.05) reduction in protein β-catenin levels when compared to the DMH-treated groups (Fig. 8).

**The effect of *Ferula assa-foetida* hydroalcoholic extract on ACF formation**

No tumor was observed macroscopically and microscopically in any experimental groups at 8<sup>th</sup> months. In DMH-treated group (Group 2), the size of ACs was 2–3 times larger than the crypts observed in the surrounding normal tissue with a slit-like opening (Figs. 9a, b, respectively). AC was shown thickened epithelia that stained darker than normal crypts. They were raised and a large pericryptal zone was present around them (Fig. 9b). In the chemo preventive (Groups 3 and 4) and chemotherapeu-
tic groups (Groups 5 and 6) treated with *F. assa-foetida* hydroalcoholic extracts, the formation of large ACF was suppressed and the ACF were smaller and mostly contained two and three aberrant crypts in each focus (Figs. 9 c–f). There was no dysplasia, adenoma, or adenocarcinoma in ACs in all groups.

The quantitative results of the total number of ACF and the total number of ACF with 4 or more ACs in the distal one third and the proximal two thirds of colon for all experimental groups are presented in Table 1. In the distal one third, the ACF formation was found to be significantly higher in DMH-treated group (Group 2) as compared to the control group (Group 1) (*P*<0.05). Whereas, the administration of *F. assa-foetida* extract in the chemopreventive and chemotherapeutic groups to DMH-treated rats caused a significantly (*P*<0.05) decrease in the total number of ACF in the colon of rats. Also, the same results achieved about ACF with 4 or more ACs (Table 1). In the proximal two thirds part of colons, the ACF formation was shown to be significantly (*P*<0.05) higher in the DMH-treated group (Group 2) as compared to the control group (Group 1) (*P*<0.05). In contrast, a significantly (*P*<0.05) decrease

Table 1: The effects of *F. assa-foetida* hydroalcoholic extract on DMH-induced aberrant crypt foci (ACF) formation in the rat colon.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total number of ACF in colon (part c)</th>
<th>Number of ACF ≥ 4ACs in colon (part c) (malignancy index)</th>
<th>Total number of ACF in colon (part a+b)</th>
<th>Number of ACF ≥4ACs in colon (part a+b) (malignancy index)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0±0</td>
<td>0±0</td>
<td>0±0</td>
<td>0±0</td>
</tr>
<tr>
<td>DMH</td>
<td>17.4±0.97*</td>
<td>6.8±0.86*</td>
<td>13.6±2.18* *</td>
<td>4.3±1.3 *</td>
</tr>
<tr>
<td>P6.25</td>
<td>5±1.44**</td>
<td>0.8±0.58**</td>
<td>4.66±1.66** *</td>
<td>0.33±0.13 **</td>
</tr>
<tr>
<td>P12.5</td>
<td>11.6±3.04**</td>
<td>3.8±1.35**</td>
<td>3±1.52**</td>
<td>0.66±0.46 **</td>
</tr>
<tr>
<td>T6.25</td>
<td>5.75±2.17**</td>
<td>1.5±0.28**</td>
<td>5.5±5**</td>
<td>1±0**</td>
</tr>
<tr>
<td>T12.5</td>
<td>7.25±1.31**</td>
<td>2±0.64**</td>
<td>2±0.57**</td>
<td>0.66±0.33**</td>
</tr>
</tbody>
</table>

ACF: Aberrant crypt foci; AC: Aberrant crypt; Malignancy of the induced lesion (malignancy index) was expressed as the number of ACF with 4 or more aberrant crypts (ACF≥4ACs). The colon was divided into proximal (a+b), and distal (c) parts. *P*<0.05 is considered significantly different from control group within each parameter; **P*<0.05 is considered significantly different from DMH-treated group within each parameter.
in the total number of ACF in all treatment groups with *F. assa-foetida* extract was observed (Table 1). Furthermore, there was a significantly reduction of ACF with 4 or more ACs in the all treatment groups (Table 1) (P<0.05).

**Discussion**

Our previous studies reported that several natural sources such as *Zataria multiflora* essential oils, *Nigella sativa* seed powder and caraway essential oils could inhibit colon cancer induced by DMH in experimental animals by their effect on the activities of hepatic detoxification enzymes, (GST and CYP1A1) and β-catenin protein level [29,30,32,33]. In followings, this study was practically conducted to investigate, for the first time, the colon chemopreventive and chemotherapeutic activities of *F. assa-foetida* hydroalcoholic extract in rat model colon carcinogenesis induced by DMH.

DMH is highly toxic and carcinogenic affected the number of body organs including liver [34]. DMH has a major role in the chemicals, drugs and carcinogens metabolism reported to elicit hepatic oxidative stress and alter the activities of antioxidant and detoxification enzymes during extra hepatic tumorigenesis [35,36]. Additionally, it is metabolized by cytochrome P<sub>450</sub> in the liver to azoxy-methane (a known colon carcinogen), finally leading to the generation of methylidiazonium ions and carbonium ions, which are active carcinogenic electrophiles [37] that attitude their action in the colon. Our results indicated that subcutaneous injection of DMH (20 mg/kg body weight) once a week for 18 consecutive weeks led to hepatic damage. In addition, histopathological examinations revealed that the total numbers of ACF in the DMH group were significantly more than negative control group (P<0.05).

In the present study, we observed that the level of CYP<sub>450</sub> activity (Fig. 5) was significantly (P>0.05) increased in the liver of DMH group. Whereas, the chemopreventive and chemotherapeutic groups that treated with *F. assa-foetida* hydroalcoholic extract reduced the elevated level of CYP<sub>450</sub> enzyme (Fig. 5) induced by DMH. Moreover, GST is predominantly involved in the detoxification of xenobiotics such as DMH [38], carcinogens, free radicals and peroxides, by conjugating the toxic substances with GSH, ultimately protecting cells and organs against carcinogen-induced toxicity [39]. In connection, we found the increasing GST activity (Fig. 6) and protein (Fig. 7) together followed by reducing hepatic GSH (Fig. 2) as a substrate in DMH treated rats. The results indicated that that *F. assa-foetida* hydroalcoholic extracts (6.25 and 12.5 doses) as a chemopreventive and chemotherapeutic agents effectively protected the animals against DMH-induced hepatic destruction, as evidenced by returning the hepatic GSH and GST levels (Figs. 2, 6, 7). Modulating the activity of GST and GSH helps in maintaining the reduced milieu of the cell and is involved in the detoxification of various xenobiotics including carcinogens which they behaves as an antioxidant and protects biological systems [40,41]. Moreover, the remarkably elevation of FRAP (Fig. 3) as an important factors in the oxidative stress/antioxidant balancing was observed. In addition, no change in the TBARS level (as an indicator of MDA) in DMH-treated rats may be due to increased FRAP level, indicating compensatory increased of plasma antioxidants which is leaded to increased resistance and/or decreased susceptibility of the liver to free radical attack [42]. But treatment of rats with *F. assa-foetida* hydroalcoholic extracts as a cancer chemopreventive and/or chemotherapeutic agent significantly reduced the amount of FRAP level (Fig. 3). A study showed that ginger due to its ability to scavenge free radicals and toxic carcinogenic electrophiles which may be the cause for the enhanced antioxidant activities in the colon and intestinal tissues which are proved the excellent chemo-
preventive efficacy of ginger, against DMH induced colon carcinogenesis [42]. Furthermore, In a study conducted by Ansil et al., 2013, chemoprevention of colon tumorigenesis by Amorphophallus campanulatus tuber methanolic extract may be the enhancement of antioxidant enzyme systems in the liver and thereby the metabolic disposal of carcinogenic DMH metabolites [43].

Moreover, the level of colonic beta-catenin increased due to DMH injection was diminished as a result of administration of F. assa-foetida hydroalcoholic extracts as chemopreventive and chemotherapeutic compounds (Fig. 8). Histological observations of liver tissue are too correlated with the above biochemical findings as the number of ACF formation in colon was significantly reduced after treatment rats with the extracts (Table 1). Methylazoxymethanol decomposition leads to methyldiazonium ion formation and methylate cellular components such as DNA in colonic epithelial cells resulting in β-catenin gene mutation [44]. In the nucleus, it binds to the transcription factor TCF/LEF and thereby stimulates the expression of various genes [45]. In colorectal cancer, the protein level of β-catenin rises through mutation in β-catenin or APC prevents the phosphorylation and consequently β-catenin proteasomal degradation, thus leading to β-catenin/TCF/LEF complexes’ accumulation in the nucleus and activation of target genes transcription, such as cyclin D1 and c-myc [46–48]. Our previous findings also validated the colon chemopreventive activities of caraway essential oils and seed powder as well as Nigella sativa seed powder in DMH-induced colon tumors through the modulatory effect of the DMH-metabolizing enzymes and β-catenin protein level [29,30,32,33]. Indeed, based on our results, the effect of the administration of the extract at the both (chemopreventive and the chemotherapeutic) groups against DMH induced colorectal tumor genesis was similar. In connection, all the similarity data were obtained from the different biochemical tests like GSH, FRAP, MDA, GST (activity and protein) and CYP450 activity as well as histopathological studies were confirmed.

Recent study confirmed that the natural products contained antioxidant compounds which can protect the organism against these harmful pro-oxidants by a complex system of enzymatic antioxidants, nonenzymatic antioxidants and detoxification enzymes [49]. The biochemical evidence from our study clearly exhibited that F. assa-foetida hydroalcoholic extract could modulate the DMH-induced oxidative stress that might be attributed to its main chemical compositions. Also, recent pharmacological and biological study showed that F. assa-foetida has antioxidant properties which may be related to the natural antioxidants such as Eremophilene and δ-cadinene [50,51]. These compounds act as blocking agents at the initiation stage, influence the metabolism of procarcinogens by modulating the expression of cytochrome Pα enzymes involved in their activation to carcinogens and also facilitate their excretion by increasing the expression of phase II conjugating enzymes and may also limit the formation of initiated cells by stimulating DNA repair [52].
Conclusion

Our present data strongly suggested that the administrations of F. assa-foetida hydro alcoholic extracts caused the chemopreventive as well as chemotherapeutic effects against colon cancer incidence by modulating the DMH-metabolizing enzyme activities such as CYP450 and GST and oxidative stress/antioxidant parameters, i.e., GSH, FRAP concomitant with decreased level of β-catenin protein. These results prove the excellent efficacy of the herb at chemo preventive and chemotherapeutic properties, against DMH induced colon carcinogenesis.

Conflict of Interest: The authors have no conflict of interest.

References


