Journal of Food and Dairy Sciences

Journal homepage & Available online at: www.jfds.journals.ekb.eg

Therapeutic Effect of Pomegranate (*Punica granatum)* Juice and Peel Water Extract on Colon Cancer in Experimentalrats

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ABSTRACT

This study aimed to identify the effect of pomegranate juice and peel water extract in preventing colon cancer in experimental rats. Twenty five female experimental rats(*Sprague Dawley strain*) were classified into fivegroups. Colon cancer was induced in all groups by Azoxymethane (AOM) dissolved in 0.9% NaCl, injected subcutaneously for 2 weeks at a dose of 20 mg/kg/week and treated with (5-FU) (12.5 mg/kg), except for Group 1 (normal control).The chemical composition, mineral content and antioxidants of pomegranate peel juice and extract were estimated. The results of the chemical analysis showed that pomegranate juice and peel extract contained moisture, protein, fat, ash, carbohydrates, fiber, and minerals (Ca, Mg, Na, K, P, Zn, Fe, Mn, Cu), antioxidants phenols (280.70,242.70 mg/100g) and flavonoids (186.90 , 51.52 mg/100 g) in the juice and peel extract, respectively. The results of the biological experiment of experimental rats groups treated with juice and peel water extractshowed asignificant increasein weight gain, food intake , feed efficiency ,blood hemoglobin (HB) , measurement of blood hematocrit (PCV) , Red blood cell counts (RBC) ,and high density lipoprotein cholesterol (HDL-c), decreasing anti-inflammatory enzyme (Cox-2) , Prostaglandin E2 (PGE2) and cytochrome P (cytoP450), while showed significant decrease in total Cholesterol (TC) and Triglycerides (TG) ,nitric oxide (NO) , Interleukin-1 (IL-1) , tumor necrosis factor (TNF-α) compared with other positive groups(+ve). It can be recommend that consumption of pomegranate juice and peel water extract may be beneficial for those which suffering from colon cancer .

Keywords: Colon cancer, 5-Fluorouracil (5-FU),pomegranate juice and peel water extract, Azoxymethane (AOM).

INTRODUCTION

Cancer is defined as the abnormal division of normal cells in an uncontrollable manner in various tissues of the body. These cells are called precancerous, malignant, or cancer cells. These cells can spread to normal body tissues. Many cancers are named after the tissues in which the malignant cells began to divide, for example (breast, lung, colon). (Meena., 2020).

Colon cancer is the most common cancer in the world, as it ranks third among the types of cancer causing death (Lidia *et al*., 2020) .Globally 1.80 million new instances of colorectal cancer (CRC) had been identified in USA, approximately, 145,600 instances of CRC are identified annually. Out of them 1,014,200 instances are colon cancers and the rest are rectal cancers (Monjur ., 2020).

colon cancer in Egypt recorded a rate of 6.5% of all cancerous tumors, as it ranked sixth among the incidence of tumors, according to the statistics of the National Cancer Institute at Cairo University. The incidence rate was 4.2% among guys and 3.8% among females (Ahmed *et al*.,2021).

(*Punica granatum)* referred to Pomegranate, the original home of the pomegranate is Iran. It is also grown in tropical and subtropical areas. Pomegranate has been known since ancient times,and the interest in its cultivation is due to its importance to health (Marco *et al*.,2019).

Anthocyanins and flavonoids are compounds found in pomegranate juice that have antioxidant activity and are what give the juice its distinctive color.Several other compounds found in pomegranate juice in high levels are hydroxycinnamic acids (chlorogenic acid, b-coumaric acidandcaffeic acid),including vit.(B1; B2; C; E and A) ,proanthocy anidins, catechins and ellagitanninssuch as punicalin and punicalagina. It also found different types of sugars (sucrose , glucose and fructose)(Coronado et al.,2021).The plant compounds present in pomegranate juice act as an antimutagenic, antioxidant, antiviral, antisporogenic, antiobesity, and neurodegenerative disease amelioration (Ahmed *et al*.,2022).

Pomegranate peel extract contains astringent compounds and is used for medicinal purposes, because it contains plant compounds, and therefore it should not be treated as agricultural waste(Usha *et al*.,2020).There is a lot of research on the antioxidants, anticancer, and anti-inflammatory found in pomegranate, and the ability of pomegranate to treat and prevent cancer, cardiovascular disease, and diabetes (Sibel .,2020). Pomegranate peel extract contains many bioactive compounds, including anthocyanidins (cyanidin, pelargonidin, delphinidin) polyphenols, ellagitannins and flavonoids (kaempferol, quercetin, luteolin)(Mariuset *al*.,2021).

Azoxymethane (AOM) is a carcinogen that activates the metabolism to form DNA-reactive compounds. The metabolism of those compounds involves several biosynthetic metabolic enzymes, which proceed through several steps of N-oxidation and hydroxylation (Daniel *et al*., 2009) .

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DOI: 10.21608/jfds.2023.181435.1089

5-fluorouracil (5-FU) has been used for nearly fifty years to treat colon cancer, especially for those with stage third and some other stages of colon cancer, and it also has harmful side effects during prolonged use. (Yasmin *et al* ., 2019).

Therefore, the present study aimed to investigate the effect of pomegranate juice and peel on general health status, and its therapeutic effect on the colon cancer rats .

MATERIALS AND METHODS

Pomegranate (*Punicagranatum)*: was purchased from a local market, El-Mansoura, Egypt.

Azoxymethane(AOM): was obtained from El- Gomhoria Company for chemicals, El-Mansoura, Egypt.

fluorouracil (5-FU) :was bought from at a pharmacy, EL-Mansoura, Egypt.

Experimental rats: Twenty five female rats weighing (205± 5 g) were obtained from the faculty of pharmacy, Mansoura University. All the biological experimental procedures were applied according to Internationally Ethical Guidelines for the care and use of laboratory animals. And permission for the experiment was obtained from the Research Ethics Committee at the Faculty of Specific Education, Mansoura University .The experiental animals were kept beneath observation for five days prior the start of the experiment for adaptation and fed on basal diet according to (Reeves *et al.*,1993).

Methods

Preparation juice of pomegranate: the fruits have been rinsed and peeled. They were juiced using an electric mixer (Braun) and stored immediately at -20 °C (Samah*et al*.,2016).The juices were used in the treatment of those rats exposed to colon cancer (2.5 ml/kg/day, by oral gavage) (Wael *et al*.,2020) .

Preparation Peel water extract of pomegranate: The fruits were washed with renewed water. It was peeled with a knife to get the rind. The peels were air-dried for four days under the shade, and the peels were ground using an electronic mixer (Braun). Dried and ground peels were extracted by cold soaking (10 g peels in 100 ml distilled water) for 72 hour. the extract stored in a refrigerator at 4ºC (Ejiofor *et al*.,2016). Using peels extract for treatment of those rats which were exposed to colon cancer was supplied (1.5 mL /kg/day; by oral gavage) (Mostafa *et al*.,2012).

Chemical Analyses

Moisture, protein ,fat content ,ash and crude fibers contents were determined according to the method described in the A.O.A.C (2000). T.carbohydrates were calculated by difference. Ca, Na, K and Cu was determined by (Peterburgski.,1968) . Mg, Zn, and Mn was determined by (Pellet and Young.,1980) .Total Fe was determined by (Chapman *et al*.,1982) .T. phosphorus was determined by (Peters *et al*., 2003).

Gross photochemical:

Total phenol content of pomegranate juice and peel were determined with the Folin–Ciocalteu's reagent (FCR) according to (Slinkardand Singleton., 1977).

The total flavonoid content of pomegranate juice and peel were determined by a colorimetric method as described by (Zhishen*et al*.,1999).

DPPH radical scavenging activity was done using the reported method (Yamaguchi *et al.,* 1998) .

Experimental rats design:

The experimental animals were kept under observation for seven days before start of the experiment for adaptation and fed on basal diet. Rats were divided into five groups (5 rats each), the first group (G1) rats were fed on basal diet only and contrived as normal control group (–ve), then, about Azoxymethane (AOM) was administered dissolved in 0.9% NaCl, applied subcutaneously for 2 weeks at a dose of 20 mg/kg/week until the rats became colon cancer(Mario *et al*., 2014) and treated with fluorouracil(5-FU)(12.5 mg/kg on days 1, 3, and 5 with a repeat cycle every 4 weeks for 4 months (Yasmin et al ., 2019).Rats were divided into four groups as follows:Group(2) was fed by basaldiet only without treated and was designated as control positive groups(+ve).Group (3): rats injected with 5-fluorouracil (12.5 mg/kg on days 1, 3, and 5 with a repeat cycle every 4 weeks for 4 months (Yasmin *et al* ., 2019).Group(4):rats injected with (5-FU) and fed on (2.5 mL kg/day, by oral gavage) of pomegranate juice (Wael *et al*.,2020).Group(5):rats injected with (5-FU) andfed on (1.5 ml kg/day, by oral gavage) of pomegranate peel water extract.(Mostafa *et al*.,2012).respectively , daily for 8 weeks. The food intake was calculated daily and the body weight gain was recorded weekly (Chapman *et al*., 1959). Food efficiency ratio (FER) was calculated as FER = weight gain (g)/ food intake (g). At the end of experiment (8 weeks), rats were sacrificed. Blood samples were collected into clean centrifuge tubes to obtain the serum which used for biochemical analyses.

Biochemical Analysis:

Hemoglobin (Hb) concentration (determined using cyanmethemoglobin method) were as described by (Hewitt., 1984). Red blood cell counts (RBC) was determined as described by Brown, (1976). Measurement of blood hematocrit (PCV) was determined as described by(Bull *et al*., 2000). Cyclooxygenase-2 (Cox-2) was determined according to (Jasmeet and Sanyal., 2011) Prostaglandin E2 (PGE2): assay was performed with the PGE2 enzyme immunoassay kit (R&D Systems, Inc., MN, USA) according to the supplier's instructions. described by (Su*et al*., 2002).Cytochrome P450 (CytoP450) was determined according to (Kristina *et al*., 2012).Determination of nitric oxide (NO):Nitrite was instructed by the strategy depicted by (Green *et al*., 1982) .Interleukin-1 (IL-1) was measured by the method of (Grassi *et al*., 1991).Tumor necrosis factor (TNF-α): was determined according to (Thorell and Lanner., 1973)

Assessment of lipid profile:

Determination of Total Cholesterol (TC) : Serum cholesterol was determined according to the method described by (NIHP., 1987) .

Determination of Triglycerides (TG): Serum Triglycerides were determined according to the method described by (Fossati and Prencipe., 1982),Determination of High density lipoprotein cholesterol (HDL-c): Serum HDL-c was determined according to the method described by (Burstein *et al* ., 1970).

Statistical Analysis:

Data were statistically analyzed by SPSS computer software according to (Artimage and Berry., 1987). this carried out by analysis of variance ANOVA and follow up LSD (SPSS).

RESULTS AND DISCUSSION

Chemical composition of pomegranate juice and peel water extract:

The chemical composition of pomegranate juice are illustrated in Table (1). Moisture, protein, fat , ash, carbohydrate and fiber were (82.50, 1.02, 0.17, 1.50, 11.31and3.50%) respectively, while pomegranate peel water extract contained(7.27, 3.74, 0.85, 4.32, 66.51 and17.31%)respectively. As well as, the determination of some mineral such as Calcium, Magnesium, sodium , potassium, phosphorus ,zinc , iron, manganese and cuprum from pomegranate juice (11.05, 15.24, 3.42, 6.92, 18.68, 1.35, 1.31 , 0.94 and 0.63) mg/100g respectively, while pomegranate peel water extract (297.5, 0, 65.4, 136.4, 112.3, 1.34, 5.64, 0.83 and 0.56) mg/100g respectively. These data are confirmed with Salah *et al* .,(2002) who indicated that the pomegranate juice contain water, sugar, protein, fat and ash (84.57, 14.1,1.05, 0.15 and 0.33%)respectively. El-Hamamsy *et al* .,(2020) cleared that the chemical composition of pomegranate peel extract it contained 0.85% fat, 4.22 ash, Protein 8.97% , moisture 6.95% , Fiber 19.41and Carbohydrates 59.60% . Saeed *et al* .,(2013) indicated that the pomegranate minerals content Calcium, Magnesium, sodium, potassium, Phosphorus, Zinc, iron, Manganese and cuprum (10.82, 15.63, 3.51, 6.56, 19.30, 1.44, 1.54, 1.69 and 0.86mg/100g), respectively. Rowayshed *et al*.,(2013) indicated that the Pomegranate peel powder minerals contents Calcium, potassium, Phosphorus, sodium, iron, Zinc and cuprum (338.5, 146.4, 117.9 , 66.4, 5.93, 1.01 and 0.60 mg/100g) ,respectively.

Table 1. The chemical composition of pomegranate juice and peel water extract

Pomegranate	Moisture %	C. Protein %	T. Fat %	Ash %	T. carbohydrates %	C. Fiber %	Ca mg/ 100g	Mg mg/ 100g	Na mg/ 100g	K mg/ 100g	P mg/ 100g	Zn mg/ 100g	Fe mg/ 100g	Mn mg/ 100g	Cu mg/ 100g
Juice	82.50	1.02	0.17	1.50	11.31	3.50	11.05	15.24	3.42	6.92	18.68	1.35	1.31	0.94	.630
Peel extract	7.27	3.74	0.85	4.32	66.51	17.31	297.5	--	65.4	136.4	112.3	1.34	5.64	0.83	0.56

Calcium (Ca), Magnesium(Mg), sodium (Na), potassium(K), Phosphorus (P), Zinc (Zn), iron(Fe), Manganese(Mn),and cuprum (Cu) mg/100mg.

Phytochemical screening total phenol, total flavonids and DPPH % of pomegranate juice and peel water extract:

Data presented in Table (2) showed the pomegranate juice contained total phenol and total flavonoids being 280.7 and 186.9 mg/100gm respectively and the pomegranate peel water extract contained 242.70 and 51.52 mg/100g respectively, while the DPPH radical-scavenging activity of pomegranate was juice and peel water extract were 23.2 and 64.32% respectively. The results in this study are consistent with those reached byAmjad *et al* ., (2013) who established that the phenol, flavonoid content and DPPH% of pomegranate were determined(348, 225and 19.4) respectively .Mouna*et al* ., (2017) reported that the Pomegranate peel consists of phenols varying from (209.83 to 202.11) and the total flavonoids ranged from (9.98 to 15.25) Quercetin mg/g in water, DPPH free radical scavenging activity, radical scavenging range from 71.11 to 84.16%.

Effect of pomegranate juice and peel water extract on body weight gain, feed intake and feed efficiency on normal control and groups of rats suffering from colon cancer.

Data presented in Table (3) showed that the non-treated rat group (+ve) showed significant decrease in final weight ,weight gain , food intake and feed efficiency ratio (FER) compared with normal group (-ve) . The colon cancer ratgroup(4) treated with (5-FU) +pomegranate juice showed significant decrease in final weight, weight gain, feed intake, feed efficiency ratio (FER) compared with normal group (-ve) .while showed a significant increase in final weight ,weight gain and feed intake, and showed non-significant in feed efficiency ratio (FER) compared with positive group (+ve).On the other hand showed significant increase in final weight and weight gain, while showed non-significant in feed intake and feed efficiency ratio (FER) compared with (5-FU) group. Colon cancer rat group(5) treated with (5-FU) +pomegranate peel showed significant decrease in final weight, weight gain, feed intake and feed efficiency ratio(FER) compared with normal group (-ve) .Also, showed a significant increase in final weight, weight gain and feed intake, while were observed non-significant in feed efficiency ratio (FER) compared with positive group (+ve).On the other hand showed an increase in final weight and weight gain, while were observed non-significant in feed intake and feed efficiency ratio (FER)compared with (5-FU) group.The results in this study are consistent with those reached by Saravana*et al*., (2012) said that histopathological studies of rat colon induced by azoxymethane showed significant decrease in the amount of cancerous cells and increase in feed intake and weight gain.

Table 2. The phytochemical screening, Total phenol, Total flavonid and DPPH % of pomegranate juice and peel water extract

Samples Bioactive compounds	Pomegranate juice mg/100g	Pomegranate peelextract mg/100g
T.phenol	280.70	242.70
T.flavonoid	186.90	51.52
DPPH %	23.20	64.32

Table 3. Effect of pomegranate juice and peel extract on body weight gain, food intake and feed efficiency on normal control and groups of rats suffering from colon cancer.

Variables Rat Groups	Initial weight (g)	Final weight (g)	Weight Gain (g)	Food Intake g/day	FER (g)
G1: Normal Control (-ve)	b 208.00 ±2.68	a 235.32 ±2.58	a 27.33 ±2.79	a 23.11 ±1.10	a 0.011 ±0.23
G2: positive groups(+ve)	a 207.17 ±4.49	d 189.33 ±2.58	f -17.84 ±2.99	c 18.10 ±1.51	b -0.0098 ±0.2
G3: (5-FU) (12.5 mg/kg)	a 209.25 ±3.54	e 195.00 ±3.04	e -14.25 ±2.03	b 19.00 ±0.70	b -0.0075 ±0.24
G4: (5-FU) + Pomegranate juice(2.5 mL)	a 205.17 ±2.40	c 192.40 ±4.10	cd -12.77 ±1.90	b 19.00 ±0.80	b -0.0067 ±0.25
G5: (5-FU) + Pomegranate peel extract (1.5 mL)	a 205.33 ±4.55	b 198.45 ±2.70	b -6.88 ±1.50	b 19.20 ±1.29	b -0.0036 ±0.30

Mean± SD values in each column having different superscript (a, b, c, d...) are significantly different at P < 0.05

Effect of pomegranate juice and peel extract on levels of blood hemoglobin (HB) , measurement of blood hematocrit (PCV) , red blood cell counts (RBCs) in blood samples from the normal control group and groups of rats suffering from colon cancer.

Data illustrated in Table (4) indicated that the non-treated rat group(2) showed significant decrease in HB ,PCV and RBC_s compared with normal group (-ve) .The colon cancer rat group(4) treated with (5-FU) + pomegranate juice was showed significant decrease in HB and PCV, while was documented non-significant in RBC_s compared with those of normal control (-ve) while showed significant increase in HB, PCV and RBC_s compared with positive group (+ve).Followed by significant decrease in HB, non-significant in PCV and a significant increase in RBC_s compared with (5-FU) group, while the colon cancer rat group(5) which treated with (5-FU) +pomegranate peel extract showed a significant decrease in HB,PCV and RBC_s compared with normal control (-ve).Also, showed a significant increase in HB and RBC_s, while was observed with non-significant in PCV compared with positive group (+ve), but showed significant decrease in HB and PCV, while showed anon-significant in RBC_s value compared with(5-FU) group. The results in this study are consistent with those reached Eirini *et al.*, (2017) who reported that the consuming pomegranate for two weeks significantly increased red blood cell count, hemoglobin levels, and hematocrit levels with non significant changes in factors related to metabolic health and sore in healthy individuals.

Table 4. Levels of blood hemoglobin (HB) , Measurement of blood hematocrit (PCV) , Red blood cell counts (RBCs) in blood samples from the normal control group and groups of rats suffering from colonic treated with pomegranate Juice and peel extract .

Variables Rat Groups	HB g/dl	PCV %	RBCs
G1: Normal Control (-ve)	a 13.40 ± 0.14	a 52.34 ± 6.06	a 4.66 ± 023.
G2: positive groups(+ve)	f 6.30 ± 0.40	d 28.80 ± 3.50	d .131 ± 0 .32
G3: (5-FU) (12.5 mg/kg)	bc 12.09 ±0.1	c 33.74 ±3.40	b 3.45 ±0.15
G4: (5-FU) + Pomegranate juice(2.5 mL)	d 9.80 ±0.10	c 33.70 ± 3.00	a 4.10 ± 0.20
G5: (5-FU) + Pomegranate peel(1.5 mL)	d 9.30 ± 0.20	d 28.40 ± 1.20	b 3.40 ± 0.08

Mean± SD values in each column having different superscript (a, b, c, d...) are significantly different at P < 0.05

Effect of pomegranatejuice and peel extract on Total Cholesterol (TC) , Triglycerides (TG) and High density lipoprotein cholesterol (HDL-c) in groups of rats with colon cancer.

The obtained results in Table (5) illustrated that highly significant elevation in T.C and TG, concurrent with highly significant reduction in HDL-c in positive group rats as comparable with (-v) control. While colon cancer rat group(4) which treated with (5-FU) + pomegranate juice showed a significant increase in T.C and TG, and decrease in HDL in compared with normal group (-ve) .observed decrease in T.C and TG, followed by increase in HDL in compared with positive group (+ve). On the other hand showed a significant decrease in TC and TG, observed with non-significant in HDL compared with (5-FU) group. While colon cancer rat group(5) treated with (5-FU) + pomegranate peel extract showed a significant increase in TC and TG compared with normal control group (-ve) ,while showed significant decrease in TC and TG, but showed a significant increase in HDL compared with these of positive group (+ve) and (5-FU) group. This study are similar to that obtained by Amir., (2011) scientific studies suggests that pomegranate juice may activate paraoxonase 1, which raises high-density lipoprotein (HDL) and lowers low-density lipoprotein (LDL) for aggregation and oxidation.

Table 5. Effect of pomegranate juice and peel extract on lipid profile.

Variables Rat Groups	TC	TG	HDL
G1: Normal Control (-ve)	c 48.90 ± 1.96	c 52.06 ± 1.99	a 48.07 ± 0.79
G2: positive groups(+ve)	a 77.30 ± 8.11	a 113.08 ± 2.00	e 10.16 ± 1.12
G3: (5-FU) (12.5mg/kg)	a 68.62 ±7.14	a 60.53 ±3.42	c 12.63 ±1.50
G4: (5-FU) + Pomegranate juice(2.5 mL)	b 51.47 ± 3.02	b 54.89 ± 2.81	d 13.60 ± 1.40
G5: (5-FU)+Pomegranate peel extract(1.5 mL)	b 50.93 ± 1.13	b 56.95 ± 2.72	b 16.12 ± 1.09

Mean± SD values in each column having different superscript (a, b, c, d...) are significantly different at P <0.05 .

Anti-inflammatory enzyme (Cox-2) , Prostaglandin E2 (PGE2) and cytochrome P (cytoP450) in tissuesof normal control group and groups of rats with colon cancer treated with pomegranate juice and peel extract .

Data in Table (6), cleared that elevated significantly in Cox-2, PGE2 and cytoP450 in (+v) group as comparable to (-v) control. While colon cancer rat groups (4&5) which treated with (5-FU) +pomegranate juice and (5-FU) + pomegranate peel extract showed a significant increase in Cox-2, PGE2 and cytoP450in compared with normal group (-ve) , but showed a significant decrease inCox-2, PGE2 and cytoP450in compared with positive group (+ve),while showed a significant decrease in Cox-2 , PGE2 and non-significant in cytoP450compared with (5-FU) group. The results in this study are consistent with those reached by many authors: Hamid *et al.*, (2012) indicated that the pomegranate stimulates cell differentiation, has anti-mutagenic and inhibitory effects on vital enzymes for example CYP450and COX. Marco *et al.*, (2022) showed that consumption of pomegranate fruit extract (34 mg/kg body weight) negatively affected the activity of both COX-2and COX-1 enzymes, and reduced the level of PGE2.

Table 6. Levels of anti-inflammatory enzyme (Cox-2) , Prostaglandin E2 (PGE2) and cytochrome P (cytoP450) in tissues of normal control group and groups of rats with colon cancer treated with pomegranate juice and peel extract.

Variables Rat Groups	Cox-2 µ/mg	PGE2 pg/mg	CytoP450 ng/mg
G1: Normal Control (-ve)	f 0.97 ± 0.15	e 186.73 ± 11.30	d 6.03 ±0 .23
G2: positive groups(+ve)	a 22.10 ±2.01	a 383.74 ± 22.30	a 10.91 ±0 .24
G3: (5-FU) (12.5mg/kg)	b 6.03 ±1.22	b 285.53 ±19.84	b 8.38 ±0.42
G4: (5-FU) +Pomegranate juice (2.5 mL)	d 4.02 ± 0.49	c 258.24 ± 4.55	b 8.89 ± 0.08
G5: (5-FU) + Pomegranate peel extract (1.5 mL)	d 4.12 ± 1.22	c 250.12 ± 16.12	b 8.51 ± 0.40

Mean± SD values in each column having different superscript (a, b, c, d...) are significantly different at P < 0.05

Levels determination of nitric oxide (NO) , Interleukin-1 (IL-1) , tumor necrosis factor (TNF-α) in tissues of normal control group and groups of rats with colon cancer treated with pomegranate juice and peel

The obtained results in Table (7) indicated that the positive control group showed significant increase in NO, IL-1 and α TNF compared with normal group (-ve) .Colon cancer rat group(4) treated with (5-FU) +pomegranate juice showed a significant increase in NO,IL-1 and α TNF in compared with normal group (-ve) and significant decrease in NO, IL-1 and α TNF compared with those of positive group (+ve) and (5-FU) group. While the colon cancer rat group (5) treated with (5-FU) +pomegranate peel extract showed significant increase in NO , IL-1 and α TNF compared with normal group (-ve) , while showed significant decrease in NO and α TNF, and non-significant in IL-1compared with positive group (+ve) and (5-FU) group. The results in this study are similar to that obtained by Seher., (2009) who reported that the pomegranate juice, punicalagin, and TPT markedly suppressed tumor necrosis factor-alpha (TNFα) mediated expression of COX-2, an inducible member of COX family of regulatory proteins in HT-29 cells.

Table 7. Levels determination of nitric oxide (NO) , Interleukin-1 (IL-1) , tumor necrosis factor (TNF-α) in tissues of normal control group and groups of rats with colon cancer treated with pomegranate juice and peel extract .

Variables Rat Groups	NO pg/mg	IL-1 pg/ml	α TNF pg/ml
G1: Normal Control (-ve)	g 36.68 ± 3.98	d 16.81 ± 2.79	d 6.19 ± 1.65
G2: positive groups(+ve)	a 72.59 ± 7.35	a 44.88 ± 3.65	a 16.68 ± 2.12
G3:(5-FU) (12.5 mg/kg)	b 64.23 ±2.35	a 43.52 ±3.63	a 15.75 ±2.63
G4:(5-FU)+ Pomegranate juice (2.5 mL)	e 41.01 ± 1.27	c 33.43 ± 1.79	b 11.31 ±2 .21
G5: (5-FU) + Pomegranate peel extract (1.5 mL)	e 42.64 ± 3.23	ab 38.69 ± 2.79	b 11.24 ± 0.76

Mean± SD values in each column having different superscript (a, b, c, d...) are significantly different at P < 0.05

CONCLUSION

This study has lent credence to use of pomegranate juice and peel extract in the treatment colon cancer. This may have been thinkable due to the presence of some antioxidant components in pomegranate juice and peel extract cause of their content for bioactive compounds phenols, flavonoids and B- carotene.

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التأثيرات العلاجية لعصير والمستخلص المائى لقشر الرمان على فئران التجارب المصابة بسرطان القولون

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الملخص

يهدف هذا البحث إلى دراسة التأثير العلاجى لعصير ومستخلص قشور الرمان على الفئران المصابة بسرطان القولون لدى خمسة وعشرون من إناث الفئران تم تحفيز سرطان القولون بمادة الأزوكسي ميثان بالحقن تحت الجلد لمدة أسبوعين بجرعة 20مجم /كجم أسبوعياً وعلاجها ب5- فلوريوراسيل (5-FU) .وقد تم تقدير التركيب الكميائى ومحتوى المعادن ومضادات الاكسدة لعصيرومستخلص قشرالرمان.أظهرت نتائج التحليل الكيميائى إحتواء عصير الرمان ومستخلص القشور على الرطوبة والبروتين والدهون والرماد والكربوهيدرات والألياف والمعادن(Ca, Mg, Na, K, P, Zn, Fe, Mn, Cu) وكانت مضادات الأكسدة والفينولات (242.70-280.70 مجم/100جم) والفلافونويد (186.90 - 51.52 مجم/100جم) فى العصير والمستخلص القشور على التوالى .أظهرت نتائج التجربة البيولوجيه وجود زيادة معنوية في المجموعات المريضة التي تم معالجتها بعصير ومستخلص قشر الرمان في كلا من الوزن النهائي والوزن المكتسب ومعدل الاستفادة من الغذاء وأيضا أرتفاعًا في نسبة الهيموجلوبين وحجم كرات الدم وعدد كرات الدم الحمراء المقارنة بالمجموعة الكنترول الموجبة ، و انخفاضاً معنوياً فى TC و TG والإنزيمات مثبط الألتهاب والبروستاجلاندين وسيتوكروم ومستوى النتريك اوكسيدفبالبلازما وإنترلوكين(1)وعامل نخر الورم بالمقارنة بالمجموعة الكنترول الموجبة.يوصى بضرورة تناول عصير و مستخلص المائى لقشور الرمان لأولئك الذين يعانون من سرطان القولون لما لها من فوائد صحية.

الكلمات الداله: سرطان القولون- 5- فلوريوراسيل(5-FU) –عصير والمستخلص المائى لقشور الرمان –الأزوكسي ميثان