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In vivo: Biochemical and Biological Studies of Fennel and its Mixtures with Green Tea

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Abstract

Cardiovascular diseases occur due to the presence of by radicals which that are byproducts of metabolic pathways. The presence of these free radicals led to the search for plants that have antioxidant properties. Mixture of fennel and green tea was chosen to increase the flavonoids constituents. Combination both of fennel with green tea which, that contain high quantity of phenolics, flavonoids and alkaloids. HPLC analysis showed the high content of polyphenolic compounds especially Gallic acid (2351.62 µg/g) evidence that, the potent antioxidant assay. Rats which feeding on bad diet showed the best results in the group which treated with extract of 10% seeds of fennel with green tea comparing with control. Among the groups of the rats fed on fennel and green tea 9:1 slightly improved the liver and kidney functions of the rats that feed on high content of lipid and polysaccharides in serum, compared with that, group fed on fennel and green tea 4:1.

Keywords: Blended Cardiovascular diseases; HPLC; phenolic compounds; flavonoids

1. Introduction

Because of its aromatic fruits of fennel, which are used as a culinary spice, it is grown in tropical regions of the world [1, 2]. Moreover, ripe fruit and its essential oil are utilized as ingredients in baked goods, liqueurs, pickles, and cheese, as well as in pharmaceutical and cosmetic items [3]. Seeds of fennel are diffuse for home remedies, it useful in the treatment of some health problems specifically the digestive system. It also used for bronchitis and chronic coughs, diabetes, also treatment of kidney stones and diuretic, [4].

Fennel has so many uses and therapeutic benefits that it has been traded from one nation to another for ages. All portions are also consumed as vegetables and added to salads [5]. Fennel possesses sensory qualities including aroma and flavour in addition to its richness in carbs, sugars, minerals, and vital fatty acids [6, 7].

The polyunsaturated fatty acids from omega-6 and omega-3 have strong biological capabilities in low concentrations, which are demonstrated by their control on numerous bodily systems [8].

The most significant and historically significant medicinal beverage traded globally is green tea. The leaves of the "Camellia sinensis" plant are used to make green tea. It has several health benefits and can be made into a drink. Use of its extract in medicine. There are thousands of bioactive compounds in green tea. Polyphenols, proteins, alkaloids, amino acids, volatile chemicals, glucides, minerals, and trace elements are among the diverse chemical components of tea [9]. Among the most significant are polyphenols, which play a part in disease prevention. In addition, there are other substances including coffee, fluoride, chromium, and manganese [10].

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Green tea has been demonstrated to have antioxidant, anticarcinogenic, antibacterial, anti-inflammatory, diabetic, obesity, and importance to cardiovascular disease (CVD) properties [11].
were analyzed by DTA, FTIR, SEM, and XRD.

2. Experimental details

2.1 Materials

Chemicals

All chemicals of high grade of purity were obtained from Sigma-Aldrich

Plant collection

The plants were obtained at a local market in in Zagazig Government, Sharkia, Egypt, during July 2021 and were identified by Botany department, Faculty of Science at Zagazig University. A voucher specimen is deposited (numbers for fennel, EGY 201/80/90-5 and for green tea.

2.2. Methods of investigation

Plant extraction

Plants were dried for ten days at room temperature. Then it was ground into a fine powder. Green tea and fennel extract was extracted by alcohol, kept in a flask at room temperature for two weeks. Apart of Green tea and fennel extract was put on the Rotary apparatus (evaporation) to chemical composition analysis.

Estimation of polyphenolic compounds:

Utilizing a modified approach [12]. An Agilent 1260 series was used for the HPLC analysis. After then, separation was done using a C18 column (4.6 mm x 250 mm i.d., 5 m). Water and acetonitrile are present in this phase at a flow rate of 1 m l/min. The duration of this step, which was done in a linear gradient, was planned as follows: 12–16 min (80% A), 8–12 min (50%), 5-8 min (40%) and 0–5 min (80% A). At 280 nm, the detector is observed at many wavelengths. The injection volume for the sample solutions was 10 l, and the column's temperature was kept at 35 °C. Both the fennel and the green tea extracts contained a quantity of polyphenols, according to HPLC analyses.

Experimental Design

We used in this study 25 adult male albino rats, weighting (140±5g). We give them the water through the cages by glass tube projecting .We prepared basal diet by fine components (100 g) by [13]. After the all rats with FBG >126 mg/dl were become obesity, then divided to five groups as follows: Group 1 as control positive that, fed on basic fooder (300 gm diet). Group 2 was fed on basic fooder + (800 gm fats and 600 gm starch) to end of experiment. Group 3 was fed on basic fooder + (800 gm fats and 600 gm starch +300 gm fennel) Group 4 was fed on basic fooder of + (800 gm fats and 600 gm starch +270 gm fennel + 30 gm green tea). Group 5 was fed on basic fooder+ (800 gm fats and 600 gm starch +240 fennel + 60 gm green tea) [14-16].

Collection of samples

5ml blood in gel tubes by cardiac puncture at 15th and 30th day during dosing period. Then were centrifuged to the samples for 3000rpm for 15 minutes in centrifuge machine (Humax) .The analysis on blood fats levels were done on Humalyser 3000 by standard reagents by Human Germany. We were determined glucose, cholesterol and triglycridelevels at the end of the study.

Estimation

At the beginning and end of the experiment blood (5ml) was collected from the vein .Then Erythrocytes and plasma were separated, plasma glucose [17, 18], lipase [19], liver functions (AST, ALT and ALP) were carried out according by [20, 21], creatinine ,kidney functions [20], urea [22], uric acid [23], total cholesterol (T.C) [24], HDL- cholesterol [25], triglycerides (T.G) [26]. At the end, serum LDL-cholesterol was calculated using the equation of total cholesterol (triglycerides/5) – HDL- cholesterol.

Statistical analysis

By SPSS v.16 data was analyzed .And were expressed all values as mean±standard error and have been compared by the way of control values ANOVA and P values and <0.05 were considered as statistically significant and <0.01 as highly significant.

3. Results and Discussion

Total phenolic compounds

HPLC analysis showed the presence of Gallic acid, Protocatechuic , p-hydroxybenzoic Gentisic , Cateachin, Chlorogenic, Caffeic, Cafaiene, Epicatachin, gallate, Syringic, Vanillic, Cinnamic, Qurecetin, Ferulic, Sinapic, , p-coumaric, Rutin, Rosmarinic, Apigenin-7-glucoside, Apigenin, Kaempferol and Chrysin (**Figure 2, Table 1**) that may be responsible for its therapeutic potential. The quantities of polyphenols are shown in **Table 1**.

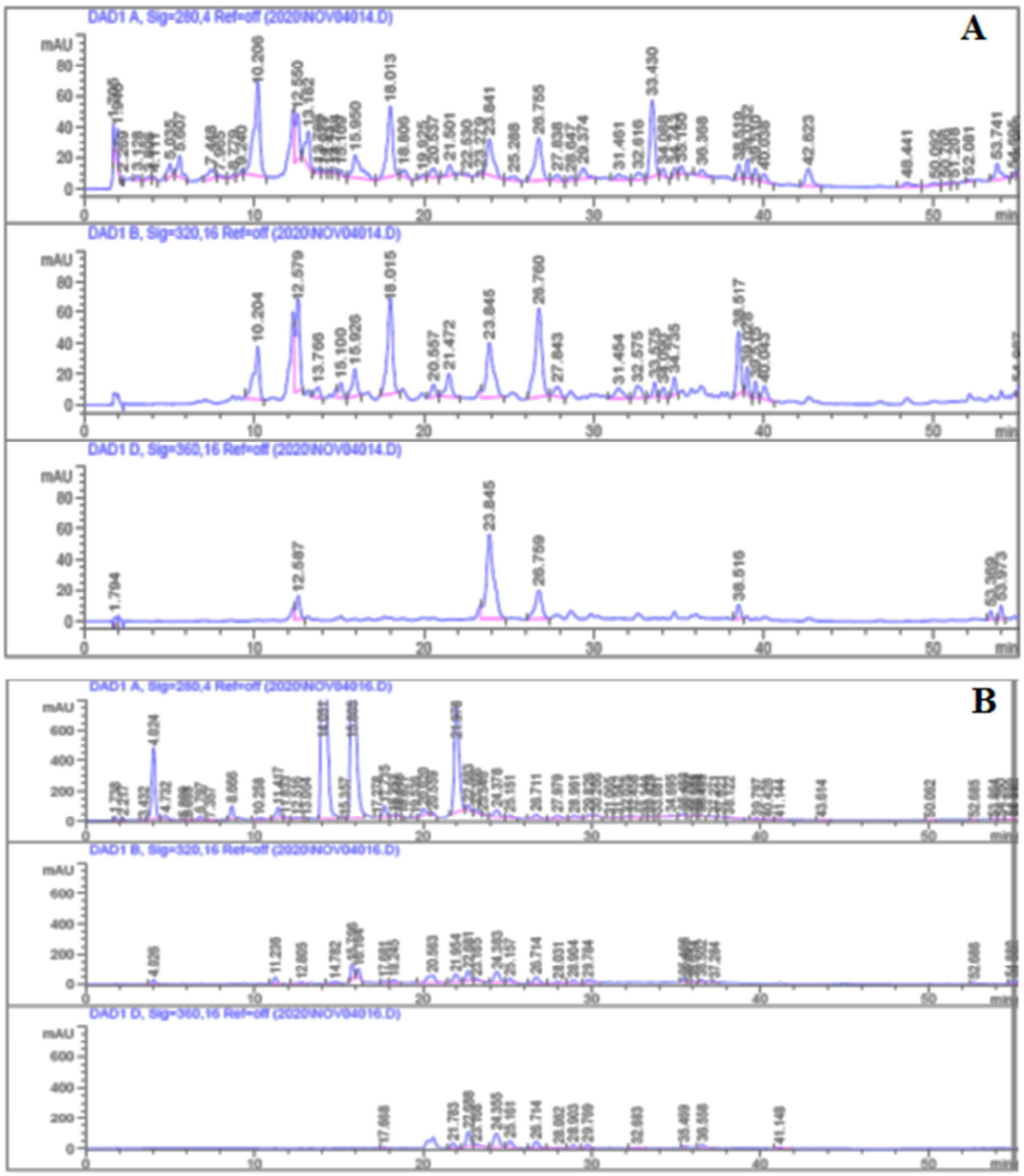
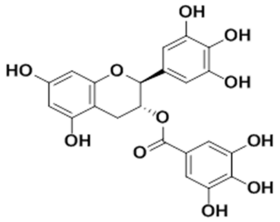


Figure 1: HPLC-MS Chromatograms of Phenolic content of :A) fennel, B) green tea

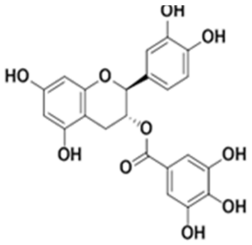
Table 1
polyphenolic compounds (µg/g) of fennel and green tea

Compound	fennel	green tea
Gallic acid	4.79	2351.62
Protocatechuic acid	ND	266.13
p-hydroxybenzoic acid	440.91	157.67
Gentisic acid	ND	ND
Cateachin	ND	1638.30

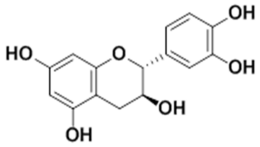
Chlorogenic acid	225.80	68.91
Caffeic acid	14.07	ND
Cafaiene	ND	37740.99
Syringic acid	6.65	ND
Vanillic acid	61.26	ND
Ferulic acid	15.48	301.97
Sinapic acid	40.66	ND
Epicatachin gallate	ND	216.85
p-coumaric acid	13.11	244.61
Rutin acid	632.68	67.86
Rosmarinic	90.27	ND
Apigenin-7-glucoside	64.31	132.68
Cinnamic acid	9.24	57.21
Qurecetin	ND	44.68
Apigenin	84.63	ND
Kaempferol	ND	ND
Chrysin	2.78	7.44



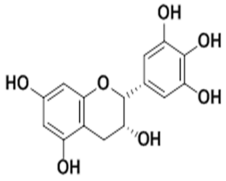
Epigallocatechin gallate



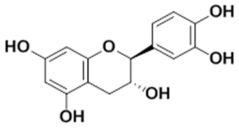
Epicatachin gallate



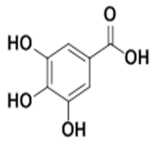
Epicatachin



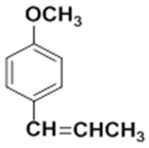
Epigallocatechin



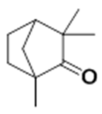
Catechin



Gallic acid



Anethole



Fenchone

Figure 2: Basic structures of different green tea catechins polyphenols

Blood Parmater:

Chemical analysis

Were found to be significantly increased in creatinine, urea , uric acid and nitrogen in rats which feeding bad diet control (+ve) see table 2, the group which treated with 10% seeds of fennel showed the best results comparing with control(-ve) (Table 4) (Figures 3&4). On the other side the bad diet caused highly increased in cholesterol (+ve), rats which feeding bad diet showed the best results in the group which treated with extract of 10% seeds of fennel with green tea comparing with control (-ve) (Table 3). A decrease in cholesterol was observed in group 4.

Table 3
Effect of fennel and green tea and ethanol extract on Serum lipid

Parameters Groups	FI (g/day) (Mean±SD)	FER (%) (Mean±SD)	BWG (g) (Mean±SD)
(G_1) Control (-)	134 ^{c} ± 6.00	59.33^{c}±2.89	58.5^{c} ± 1.50
(G_2) Control (+)	176.67^{a}±3.21	70.67^{b}±1.53	79 ^{a} ± 1.00
(G_3) fennel	161.67^{b}± 4.16	69 ^{b} ± 6.00	60 ^{c} ± 1.00
(G_4) 9:1	135.33^{c}±0.58	61 ^{c} ± 1.00	51 ^{d} ± 1.00
(G_5) 4:1	162.67^{b}±3.06	80.67^{a}±0.58	70.33^{b}±4.16
LSD	6.97	5.64	3.87

Table 2
Feed intake (FI), feed efficiency ratio (FER) and body weight gain (BWG) of rats treated with fennel and its mixtures with green tea

Parameters Groups	FI (g/day) (Mean±SD)	FER (%) (Mean±SD)	BWG (g) (Mean±SD)
(G_1) Control (-)	17.42^{a}± 0.84	5.5 ^{b} ± 0.69	0.96^{b} ± 0.10
(G_2) Control (+)	17.88^{a}± 0.73	7.9 ^{a} ± 1.78	1.42 ^{a} ± 0.34
(G_3) fennel	17.76^{a}± 0.71	9.16 ^{a} ± 0.50	1.62 ^{a} ± 0.06
(G_4) 9:1	18.26^{a}± 0.54	8.92 ^{a} ± 0.61	1.62 ^{a} ± 0.10
(G_5) 4:1	17.84^{a}± 0.81	9.46 ^{a} ± 0.85	1.68 ^{a} ± 0.14
LSD	0.97	1.32	0.23

Table 4
Effect of seeds of fennel and green tea on kidney functions

Parameters Groups	Creatinine (mg/dl) (Mean±SD)	Urea (mg/dl) (Mean±S.D)	Uric acid (mg/dl) (Mean±S.D)
(G_1) Control (-)	0.50 ^{c} ± 0.01	40.33^{b}±1.53	2.71^{bc}± 0.17
(G_2) Control (+)	0.57 ^{a} ± 0.02	53.67^{a}±2.52	4.57^{a} ± 0.61
(G_3) fennel	0.48^{c} ± 0.006	34.5^{c} ± 0.5	2.29^{c} ± 0.09
(G_4) 9:1	0.50^{bc}±0.006	36 ^{bc} ± 4	2.15 ^{c} ± 0.28
(G_5) 4:1	0.52^{b} ± 0.006	52 ^{a} ± 2	3.08^{b} ± 0.11
LSD	0.02	4.38	0.58

Table 5
Effect of fennel and green tea on liver enzymes

Parameters / **Groups**	**T.B (mg/dl) (Mean±S.D)**	**ALP (U/L) (Mean±S.D)**	**ALB (Mean±S.D)**	**ALT (Mean±S.D)**	**AST (Mean±S.D)**
(G_1) Control (-)	0.29 ^{b} ± 0.02	102.5 ^{c} ± 1.50	2.48 ^{b} ± 0.39	26 ^{c} ±2.65	108 ^{b} ± 3.00
(G_2) Control (+)	0.4 ^{a} ± 0.02	154.33 ^{a} ± 0.58	3.5 ^{a} ± 0.04	47 ^{a} ±2.00	138 ^{a} ±2.00
(G_3) fennel	0.27 ^{b} ± 0.02	64.17 ^{d} ± 1.76	2.29 ^{b} ± 0.26	25.5 ^{c} ± 0.50	79.5 ^{d} ± 0.50
(G_4) 9:1	0.26 ^{b} ± 0.03	61 ^{e} ±2.65	1.4 ^{c} ±0.20	18 ^{d} ±20	55.5 ^{e} ± 2.50
(G_5) 4:1	0.28 ^{b} ± 0.04	113.33 ^{b} ± 1.53	2.86 ^{b} ± 0.33	39.33 ^{b} ± 0.58	97 ^{c} ±3.60
LSD	0.05	3.15	0.49	3.21	4.64

Histopathological examination of heart:

With microscope, found that heart of mice on group 1 showed a normal histological structure of cardiac myocytes (Figs. 1, 2 & 3). While, heart of mice on group 2 showed congestion on myocardial (Fig. 4) and edema between the cardiac myocytes (Fig. 5). And some examined sections on group 3 showed congestion of myocardial blood (Fig. 6) and vacuolation in the wall of myocardial blood vessel (Fig. 7), whereas, while the other sections showed no pathological (Fig. 8). Furthermore, heart of mices on group 4 described no pathological in alterations except congestion of myocardial blood vessels in some sections (Figs. 9, 10 & 11). It is also examined cardiac sections on group 5 manifested no pathological alterations (Figs. 12, 13 & 14).

Other water-soluble antioxidants, including flavonoids, would also have positive effects on endothelial function because of the considerable earlier research confirming the benefits of ascorbic acid on endothelial function. Green tea contains a variety of antioxidant flavonoids that are water soluble, such as quercetin, and other polyphenols, especially Gallic acid and gallate on flow-mediated dilation in the brachial artery. Participants were requested to abstain from consuming green tea and fennel throughout the trial, and subjects using antioxidant supplements were also excluded. Every individual was taking medicine for their coronary arteries [27].

Histopathological examination of kidneys:

With microscope, kidneys of mices on group 1 revealed the normal histological structure on them (**Figs. 1 & 2**). On the other hand, kidneys of mices on group 2 showed vacuolar degeneration on renal tubules (**Figs. 3 & 4**). Furthermore, kidneys of rats on group 3 showed protein cast in the lumen of some kidney tubules (**Fig. 5**), vacuolar degeneration of epithelial lining some kidney tubules and endothelial lining glomerular tuft (**Fig. 6**). While, some sections from group 4revealed no histopathological alterations (**Figs. 7 & 8**), whereas, other sections described only slight vacuolation of epithelial lining some renal tubules (**Fig. 9**). It is also, kidneys of rats on group 5 exhibited no histopathological any alterations except congestion of kidney blood vessel in some sections (**Figs. 10, 11, 12 & 13**).

In order to affect glucose metabolism, which affects how much glucose is taken up by tissues, how sensitive and secreted from -cells is insulin, and how quickly intestinal glucose is absorbed, flavonoids can interact with a variety of molecular pathways and the phosphorylation of the insulin receptor (IR), quercetin and gallic acid improve insulin signal transduction [28].

Histopathological examination of liver:

With microscope, liver of mices on group 1 showed the normal histoarchitecture of hepatic tissue (**Figs. 1 & 2**). On the other hand, liver of mices on group 2 showed vacuolar degeneration of the liver cells (**Figs. 3 & 4**), portal infiltration in inflammatory cells (Fig. 4), and portal edema, congestion of hepatoportal blood vessel and hyperplasia of biliary epithelium (**Fig. 5**). While, liver of rats on group 3 revealed congestion of central veins (**Figs. 6 & 7**). On the other hand, some liver sections on group 4 exhibited no histopathological alterations (**Fig. 8**), whereas, other sections revealed congestion of central veins (**Fig. 9**) and vacuolar degeneration of different liver cells (**Fig. 10**). It is also, liver of mices on group 5 showed low hydropic degeneration of liver cells also congestion of central vein (**Figs. 11, 12 & 13**).

Flavonoids have an oxygenated heterocyclic ring composed of two rings connected by three carbons as their basic chemical structure, especially gallic acid and its gallate has been shown to control the lipid profile in serum and the liver. Ellagic acid, which found in green tea, the most prevalent component in this subclass, reduce oxidative stress after ischemia, restore the activity of antioxidant enzymes, and improve histology by lowering inflammatory response. Polyphenol supplementation is effective in treating alcoholic liver disease, non-alcoholic fatty liver disease, drug-induced liver damage, and hepatocellular cancer. The incorporation of foods high in polyphenols is a desirable strategy when creating a nutritional diet. The government should promote their consumption. For an equilibrated diet, where variety is crucial, polyphenols and other micronutrients are crucial [29].

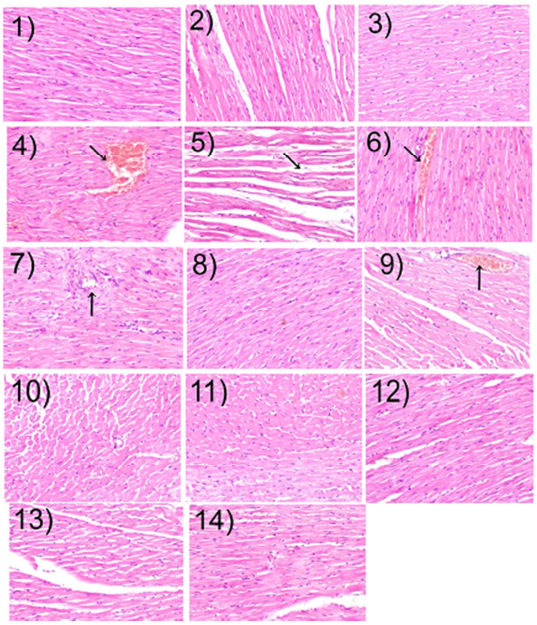


Figure 3: Effect of fennel and green tea on heart of different Experimental groups: 1) on control; 1,2,3) induced control group (bad diet) not treated ; 4,5,); treated with 10% fennel ; 6,7,8) treated with 10% fennel and green tea 9:1; 9,10,11). And group with 10% fennel and green tea 4:1; 12, 13, 14)

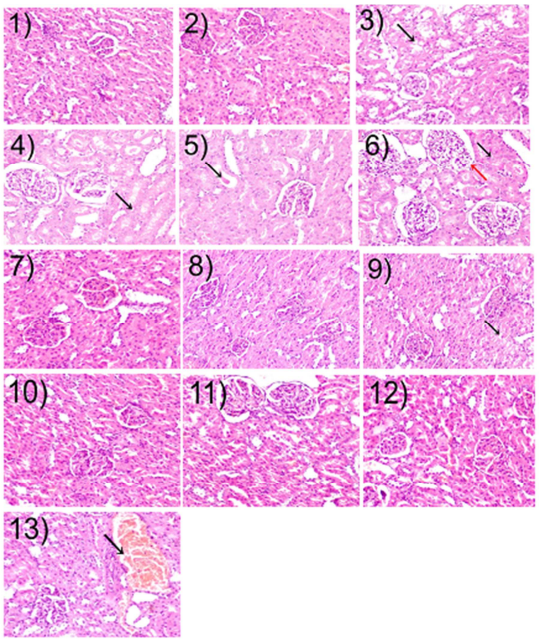


Figure 4: Effect of fennel and green tea on kidneys parts in different groups: 1) in control mices showed normal histology ; 1,2) in control group (STZ) which not treated ; 3,4,); Experimental group treated with 10% fennel ; 5,6) Experimental group treated with 10% fennel and green tea 9:1; 7,8,9) Experimental group treated with 10% fennel and green tea 4:1; 10,11,12,13)

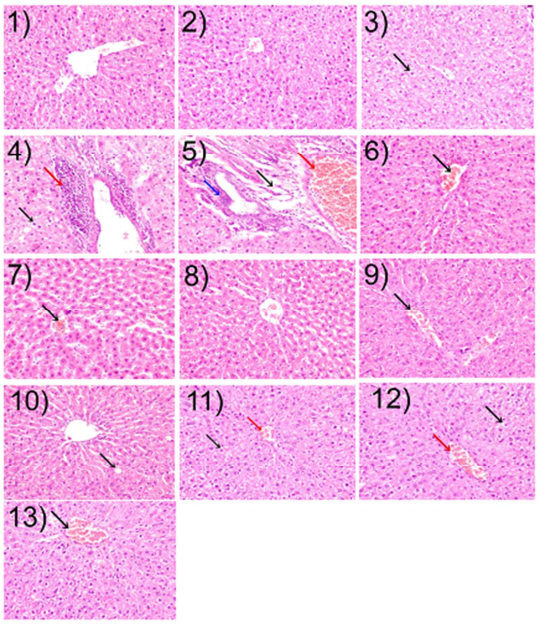


Figure 5: Effect of fennel and green tea on liver on different groups: 1) of control mices showed normal histology ; 1,2) control group (STZ) which not treated ; 3,4,5); the experimental group used with 10% fennel ; 6,7) Experimental group used with 10% fennel and green tea 9:1; 8,9,10) Experimental group used with 10% fennel and green tea 4:1; 11,12,13)

4. Conclusion

In this work, the extract of fennel and green tea was used for increase concentrations of nitric oxide to devoid of cardio vascular disease, and the effect of flavonoid compounds which of the types of polyphenolic compound to reduce the toxicity of arginine which is the main source for nitrogen and also the effect of polyphenolic with al alkaloid to increase the biological activity anti-oxidant. Gallic acid, which has a high concentration of polyphenolic components, according to HPLC study, is a powerful antioxidant. Rats who were fed a poor diet displayed the best results in the group that received a 10% fennel seed extract in green tea when compared to the control group. The liver and renal functions of the rats fed on a diet high in fat and polysaccharides in the serum were somewhat improved in the 9:1 group of rats fed on fennel and green tea compared to the 4:1 group.

5.Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

6.Acknowledgments

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