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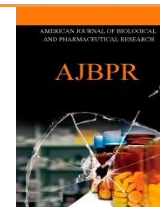

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HEPATOPROTECTIVE EFFECT OF INDIGENOUS FOENICULUM VULGARE IN ETHANOL INTOXICATED MALE AND FEMALE ALBINO RATS

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ABSTRACT

The liver performs many vital functions to eliminate toxins and harmful substances from the body. Hepatotoxic agents can directly interact with the liver through the formation of reactive radicals and consequently induce liver lesions with the progression of alcoholic liver disease. The aim of this study was to investigate the possible hepatoprotective effect of *Foeniculum vulgare* against ethanol induced hepatotoxicity in albino rats. The male and female rats with an average body weight (245 – 255g) were divided into ten groups as (Group 1 – Group 5) males and (Group 6 – Group 10) females in each group (n = 6) respectively. The rats were intoxicated with 30% of ethanol for 30 days. At the start of 31st day the rats (males: Group 4 – Group 5 and females: Group 9 – Group 10) were treated with 50 mg/kg and 1 g/kg of very fine powder of *F. vulgare* suspended in PBS. The males (Group 3) and Females (Group 8) were treated with suspension of Silymarin (50 mg/kg) for 30 days. At the end of experimental period all the animals were sacrificed to isolate the liver and blood samples. The biochemical markers such as alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), total and direct bilirubin are increased in alcohol intoxicated groups. Supplemented with *F. vulgare* in the treatment period decreased and stabilized the concentration of all parameters in male and female rats. The reduction in total protein and albumin levels of alcohol intoxicated groups were significantly increased in *F. vulgare* treated male and female rats. The results of *F. vulgare* are in consistent with the Silymarin and control rats. This study confirmed the hepatoprotective effect of *F. vulgare* in alcohol intoxicated male and female albino rats.

INTRODUCTION

The liver is an amazingly complex organ which virtually affects every physiological process of the body. It also protects our body from various injurious substances and toxic metabolic by-products, which has been absorbed from the intestinal tract. The liver has a surprising role in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease, nutrient supply, energy provision and reproduction [1, 2]. The major

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functions of the liver are in coordinating the fuel metabolism, detoxification, secretion of bile and storage of the vitamins. Any sort of damage to the liver is associated with the distortion of these metabolic functions. Thus, it is necessary for all individual to maintain a healthy liver for the overall health and wellbeing.

Liver disease is the fifth most common cause of death after heart disease, stroke, chest disease and cancer. However, unlike other major causes of mortality, liver disease rates are increasing rather than declining [3]. Liver is the primary organ responsible for alcoholic metabolism, so it is highly vulnerable to alcohol-related injuries and in the progression of alcoholic liver disease (ALD). There are considerable number of hepatotoxins that have been reported to cause the liver damage including ethanol, paracetamol, and carbon tetrachloride [4 – 7]. These agents are recognized as the most vulnerable inducers in the development of liver disease and they are often reported to cause potential hepatic damage [8].

ALD is one of the most serious consequences of chronic alcohol abuse, which includes three broad categories as fatty liver, alcoholic hepatitis and cirrhosis. Fatty liver/steatosis is the first stage of alcoholic liver damage, which is reversible with abstinence from alcohol (ethanol). Fatty liver seems to be a prerequisite to the development of alcoholic hepatitis which is considered as acute inflammation in the liver accompanied by the destruction of individual liver cells. The alcoholic hepatitis is the second progressive state of ALD [9]. Chronic levels of ALD leads to collagen deposition around central veins (cirrhosis). It further leads to increasing the risk of hepatocellular carcinoma [10]. All the tissues of the body contain oxidative enzymes but the major site of ethanol metabolism occurs in the liver.

Ethanol intake induces the mass production of free radicals in the body, which are considered to be associated with the progression of alcoholic liver disease [11, 12]. Ethanol injured the hepatocytes by lipid peroxidation of cellular membranes, and oxidation of protein along with DNA via producing free radicals. Steroids, vaccines, and chemical based drugs have been currently used in the treatment of liver diseases which have adverse side effects if administrated for long term. It is necessary to accept a point that even though enormous advances and different therapeutic discoveries are observed in the modern medicine, there is no effective drug that offers complete protection to the hepatocytes and in the treatment of liver disorders. Thus, it is necessary to identify pharmaceutical alternatives for the treatment of liver diseases, with the aim of these alternatives being more effective and less toxic. A number of research studies reported that natural products with antioxidant activity are effective to prevent the liver pathologies due to particular interactions and synergisms [13].

Plant derived natural products including flavonoids, terpenoids, phenols and steroids have received considerable attention in recent years due to their diverse pharmacological properties including antioxidant and hepatoprotective activity [14 – 16]. Phytomedicines plays positive role in maintaining wellbeing, enhancing health, and modulating immune function in preventing diseases [17]. Several studies carried out in rat models have demonstrated the hepatoprotective effect of different plant based products against ethanol intoxicity [18 – 23]. In case of hepatoprotective effect, several species have been shown to protect the liver cells and ameliorate the toxins induced hepatic lesions and confirmed their efficacy and biopotent property. One such medicinal plant used in the present study is *Foeniculum vulgare* belonging to the Umbelliferae (Family: Apiaceae) called as Fennel or Ensilal (Amharic) and Insilaalee (Oromifaa). This plant is commercially available in Ethiopia. Ethiopians tend to rely more on traditional medicine, since it is culturally entrenched, accessible, and affordable. The data base figures up to 80% of the Ethiopian population relies on traditional remedies as a primary source of health care [24].

Fennel is used as a spice and also as an important ingredient in various folklore medicines throughout the world. In Ethiopia, the boiled or roasted roots of fennel are traditionally used to treat gonorrhea, digestive disorders and infant colic. The juice of the fresh or dried leaves was used to stem nosebleeds and the plant is also known for its anti-fertility properties [25]. Females apply the aqueous extract from the leaves and young stem on their skin as a natural cleanser and to increase lactation. It is also used to treat the infections in the urinary tract [26] and as a dyeing agent alone or in combination with henna (Lawsonia inermis L.) for sheep wool.

Fennel seeds have been shown to increase milk secretion, promote menstruation, facilitate birth, and alleviate the symptoms of dysmenorrhea [27]. The antioxidant property of *Foeniculum vulgare* seeds [28], leaves [29] and fruits [30] confirmed that all parts of this plant is acting as strong phytotherapeutic agent. The shoots and leaves showed the highest levels of Vitamin E (tocopherols) and vitamin C (ascorbic acid). Fennel interacts at the membrane-cytosol interface to regenerate the oxidized form of vitamin E [31]. So based on the above objectives, the present study was designed to explore the hepatoprotective effect of *F. vulgare* against alcohol intoxicated male and female albino rats.

MATERIALS AND METHOD

Collection and identification of plants

The plant leaves of *Foeniculum vulgare* was collected in the lush green lands of Ambo University, Ambo Town, West Shoa and Ethiopia during June 2014. The plant was identified as *Foeniculum vulgare* Miller under the family of Apiaceae and the species are identified authenticated by the National Herbarium at Addis Ababa, Ethiopia.

The collected leaves were washed thoroughly in distilled water, cut into smaller pieces and dried in shade for one week and then dried leaves were kept in an air-dried

oven at 120 ºC for 48 hours. The dried leaves was powdered in ball mill and made into very fine powder and stored in airtight plastic polyethylene bottles and stored at – 20 ºC until further use as per the quality control protocol [32].

Characterization of plant leaves powder

The proximate analysis such as moisture, ash content, water soluble ash, acid insoluble ash and level of carbohydrates and secondary metabolites mainly terpenes, tannins, flavonoids, saponins, alkaloids, carbohydrates / glycosides, phenolic glycosides, crude protein, crude lipid and crude fibre were analyses as per the guidelines outlined in the literatures [33, 34]. By using acid digestion method, samples were prepared and the essential mineral contents was analysed by using Atomic absorption spectrophotometer (AA320N – Shandong, China). The total carbohydrate and nutritive values of the plant leaves powder was determined by the following formulae [35, 36].

Total carbohydrate (%) =
100 – [Moisture (%) + Ash (%) + Fat (%) + Proteins (%) + Fiber (%)] (1)

Nutritive Value (%) = [4 × Carbohydrate (%) + 4 × Proteins (%) + 9 × Fat (%)] (2)

Invivo hepatoprotective activity of *F. vulgare*: Selection of animals

The inbred Wister 60 albino rats of 30 males and 30 females weighing between 245 – 255 g were selected for this research work. The animal house was equipped with all necessary facilities to maintain the standard experimental conditions including air conditioner to adjust the room temperature 24 ± 2 ºC and 12 hour light/dark cycle. The animals were placed in polypropylene cages and the rats were fed with standard pelleted feed specially processed in the Ethiopian Public Health Institute (EPHI) and water during the experiment. All the rats were measured thrice in a week and their average body weight was recorded as weekly data throughout the experimental period. The animals were deprived of food for 24 h before experimentation, with free access to water. Analytical grade chemicals was used in this study. All the experimental studies was performed as per guidelines of the institutional ethical committee protocols for animal's research. The plant sample of *F. vulgare*, fine powder and Wister albino rat species are shown in Figure 1.

Experimental design

The albino rats of male (n = 6) and female (n = 6) was intoxicated with 30% of ethanol solution to develop the alcoholic hepatitis. The experimental design for development of the liver injury in experimental animals was illustrated in the literature [37, 38] and scheme of experimental design was as follows.

Group 1. Control male rats treated with distilled water during the ethanol (30%) intoxication and phosphate buffer saline (PBS) during the drug treatment period of 30 days.
Group 2. Ethanol (30%) intoxicated male rats (3 ml/100 gm/1 day) in orogastric doses for 30 days continuously.
Group 3. Ethanol (30%) intoxicated male rats for 30 days + treated with oral suspension of Silymarin (50 mg/kg. b.wt).
Group 4. Ethanol (30%) intoxicated male rats for 30 days + treated with *F. vulgare* (50 mg/kg. b.wt.) suspended in PBS.
Group 5. Ethanol (30%) intoxicated male rats for 30 days + treated with *F. vulgare* (1 g/kg. b.wt.) suspended in PBS.
Group 6. Control female rats treated with distilled water during the alcohol intoxication and PBS during the drug treatment period.
Group 7. Ethanol (30%) intoxicated female rats (3 ml/100 gm/1day) in orogastric doses for 30 days continuously. In all the groups' body weight was monitored weekly.
Group 8. Ethanol (30%) intoxicated female rats for 30 days + treated with oral suspension of Silymarin (50 mg/kg. b.wt.).
Group 9. Ethanol (30%) intoxicated female rats for 30 days + treated with *F. vulgare* (50 mg/kg. b.wt.) suspended in PBS.
Group 10. Ethanol (30%) intoxicated female rats for 30 days + treated with *F. vulgare* (1 g/kg. b.wt.) suspended in PBS.
The optimum drug dose of *F. vulgare* was calculated based on the body weight of the experimental animals.

Biochemical analysis

Blood sample was withdrawn from retro orbital plexus and the rats were sacrificed by diethyl ether asphyxiation. The liver of all the groups were checked for signs of apses and tumour. The wet weight of fresh liver and volume were estimated by standard procedure. The serum samples were isolated after centrifugation and the samples were directly injected into the automated clinical chemistry analyser COBAS INTEGRA 400 plus and 501 systems for the determination of albumin, total protein, ALT, AST, ALP, total and direct bilirubin. All the reagent packs are inbuilt cassettes as albumin reagent cassettes (Catalog No. 04469658 190); ALT (Catalog No. 20764957 322); ALP (Catalog No. 03039773 190); AST (Catalog No. 20764949 322); total proteins Gen.2. (Catalog. No. 03183734 190); bilirubin (Catalog No. 05589061 190) using special micro cuvettes (Catalog 21 043 862 001) was used to load the serum samples. The concentration of globulin and indirect bilirubin was calculated by the formula given here.

Globulin (g/dL) = Total protein (g/dL) – Albumin (g/dL) (3)

Indirect bilirubin (µmol/L) =
Total bilirubin (µmol/L) – Direct bilirubin (µmol/L) (4)

Statistical analysis

All the biochemical tests were done in triplicate and the results are expressed as mean ± SEM. Statistical analysis was performed by one-way analysis of variance (ANOVA) test followed by Dunnette multiple comparisons test. Statistical significance were set accordingly, [a,b,c] $P < 0.01$ as significant and [d,e,f] $P < 0.001$ as highly significant in comparison with respective groups.

RESULTS

The proximate composition and the nutritive values of the fine powder of *F. vulgare* were presented in Table 1. The nutritive value of the *F. vulgare* sample was 270.93 ± 11.83. The results depicted in Table 2 showed the higher concentration of terpenes and flavonoids followed by medium concentration of tannins, alkaloids and phenolic glycosides and the least concentration of saponins and glycosides for *F. vulgare*. Table 3 represents the quantitative analysis of calcium, cadmium, copper, iron, magnesium and zinc in the fine powder of *F. vulgare*. The increasing order of metal content was presented as follows: Ca > Mg > Cu > Zn > Fe > Cd.

The alcohol fed rats decreased their body weight in males (Group 2) and females (Group 7) compared to control (Group 1) and (Group 6) rats were presented in Table 4. The rats with *F. vulgare* at the dose of 50 mg/kg and 1 g/kg in male rats (Group 4 – Group 5) and female rats (Group 9 – Group 10) suspended in PBS for 30 days increased their body weight near to the control groups. The standard drug Silymarin males (Group 3) and females (Group 8) showed the similar effect of F. vugare.

In Table 4, it is observed that, the weight of the liver isolated from male (Group 2) and female (Group 7) alcohol intoxicated groups were increased significantly. Treatment with *F. vulgare* in males (Group 4 – Group 5) and female (Group 9 – Group 10) rats increased wound healing capacity of the *F. vulgare* against the lesions induced by 30% alcohol compared with Silymarin treated males (Group 3) and female (Group 8) rats. The results presented in Figure 2 and 3 and Table 5 showed the significant increase in concentration of ALP ($P < 0.01$), ALT ($P < 0.01$), AST ($P < 0.001$), total bilirubin ($P < 0.001$), direct ($P < 0.001$) and indirect bilirubin ($P < 0.001$) in chronic alcohol fed male and female rats. The male (Group 4 – Group 5) and females rats (Group 9 – Group 10) fed with *F. vulgare* significantly decreased the ALP, ALT and AST, total, direct and indirect bilirubin compared to Silymarin treated (Group 3) groups respectively.

The level of serum proteins in Albino rats on the treatment of *F. vulgare* after intoxication with 30% ethanol is presented in Table 6. It is observed that, a significant reduction in the serum proteins of chronic alcohol fed male rats i.e., total protein: ($P < 0.001$ and albumin: $P < 0.01$) and female rats ($P < 0.001$ and albumin: $P < 0.01$) compared to the control male (Group 1) and female (Group 6) groups. The supplementation of *F. vulgare* in the treatment period of 30 days in males (Group 4 – Group 5) and females (Group 9 – Group 10) at a dose of 50 mg/kg b.wt (Group 4) and 1 g/g b.wt (Group 5) increases the serum proteins in males and female rats respectively. The data's observed in standard Silymarin treated males (Group 3) and females (Group 8) are consistent with the *F. vulgare* and their values are near to the control group rats.

Table 1. Proximate analysis of and nutritive values of *F. vulgare*

S.No.	Parameters	Values (%)
1	Moisture	84.36 ± 0.88
2	Ash	7.53 ± 0.58
3	Acid soluble ash	1.44 ± 0.05
4	Water soluble ash	1.68 ± 0.03
5	Crude protein	4.60 ± 0.23
6	Crude lipid	12.30 ± 0.52
7	Crude fibre	26.67 ± 0.61
8	Total CHO	35.46 ± 1.56
9	Nutritive value (Calorie/100g)	270.93 ± 11.83

Table 2. Secondary metabolites of *F. vulgare*

S.No.	Phytoconstituents	Level
1	Terpenes	+++
2	Tannins	++
3	Flavonoids	+++
4	Saponins	+
5	Alkaloids	++
6	Carbohydrates/glycosides	+
7	Phenolic glycosides	++

Note: (+++) indicates high concentration, (++) medium concentration and (+) low concentration.

Table 3. Concentration of essential minerals in *F. vulgare*

S.No.	Minerals	Value (mg/g dry weight)
1	Calcium	16.5 ± 0.25
2	Cadmium	0.19 ± 0.03
3	Copper	1.69 ± 0.10
4	Iron	0.28 ± 0.05
5	Magnesium	4.47 ± 0.15
6	Zinc	0.35 ± 0.01

Table 4. Body weight, liver weight and relative liver weight changes in albino rats on the treatment of *F. vulgare* after intoxication with 30% ethanol

Groups	Body weight (g)	Liver weight (g)	Relative liver weight (g/100 g b.wt)
Males (n = 6)			
Group 1	300 ± 1.45	7.242 ± 0.022	2.41 ± 0.18
Group 2	273 ± 0.98	9.816 ± 0.025	3.60 ± 0.27
Group 3	306 ± 0.59	7.706 ± 0.016	2.52 ± 0.19
Group 4	301 ± 1.35	8.438 ± 0.169	2.80 ± 0.21
Group 5	309 ± 1.58	8.202 ± 0.019	2.65 ± 0.20
Females (n = 6)			
Group 6	294 ± 2.21	6.83 ± 0.019	2.32 ± 0.14
Group 7	270 ± 1.45	8.31 ± 0.150	3.08 ± 0.19
Group 8	304 ± 0.94	7.20 ± 0.022	2.37 ± 0.14
Group 9	302 ± 0.55	7.33 ± 0.018	2.43 ± 0.15
Group 10	310 ± 2.80	6.98 ± 0.024	2.25 ± 0.14

Table 5. Level of bilirubin in albino rats on the treatment of *F. vulgare* after intoxication with 30% ethanol

Groups	Total bilirubin (μ moles /L)	Direct bilirubin (μ moles /L)	Indirect bilirubin (μ moles /L)
Males (n = 6)			
Group 1	7.045 ± 0.47	3.35 ± 0.88	3.69 ± 0.42
Group 2	26.09 ± 1.20 ^{d}	11.59 ± 0.51^{d}	14.5 ± 1.31^{d}
Group 3	13.13 ± 1.16	5.20 ± 0.39	7.93 ± 0.78
Group 4	15.66 ± 0.44	6.81 ± 0.41	8.86 ± 0.67^{a}
Group 5	14.64 ± 0.66 ^{f,b}	7.29 ± 0.44 ^{a,e}	7.35 ± 0.97^{b}
Females (n = 6)			
Group 6	7.29 ± 0.44	5.16 ± 0.48	2.12 ± 0.1
Group 7	24.69 ± 1.23 ^{d}	9.85 ± 0.42 ^{d}	14.84 ± 0.82 ^{d}
Group 8	11.83 ± 0.86	4.82 ± 0.42	7.01 ± 0.44
Group 9	14.06 ± 0.51 ^{e,f}	6.09 ± 0.30 ^{b}	7.97 ± 0.21
Group 10	14.64 ± 0.66	6.91 ± 0.41	7.73 ± 0.96 ^{e,f}

a, b, c: The values with different letters are significantly different from each other ($P < 0.01$) and the letters d, e, f are significantly different from each other ($P < 0.001$).

Table 6. Level of serum proteins in albino rats on the treatment of *F. vulgare* after intoxication with 30% ethanol

Groups	Total Protein(g/dL)	Albumin (g/dL)	Globulin (g/dL)
Males (n = 6)			
Group 1	7.062 ± 0.24	4.62 ± 0.09	2.442 ± 0.29
Group 2	4.478 ± 0.12^{d}	2.34 ± 0.03 ^{c}	2.140 ± 0.14
Group 3	6.318 ± 0.15	3.724 ± 0.09	2.594 ± 0.10
Group 4	6.568 ± 0.24^{b}	3.876 ± 0.14	2.692 ± 0.17
Group 5	5.882 ± 0.40^{a}	3.818 ± 0.19	2.064 ± 0.32
Females (n = 6)			
Group 6	6.624 ± 0.24	4.578 ± 0.15	2.046 ± 0.17
Group 7	4.724 ± 0.09^{d}	2.830 ± 0.08^{c}	1.890 ± 0.15
Group 8	6.572 ± 0.25	4.368 ± 0.14	2.204 ± 0.22
Group 9	7.356 ± 0.28^{e}	4.682 ± 0.15^{b}	2.674 ± 0.31
Group 10	6.582 ± 0.27	4.336 ± 0.08	2.246 ± 0.19

a, b, c: The values with different letters are significantly different from each other ($P < 0.01$) and the letters d, e, f are significantly different from each other ($P < 0.001$).

Figure 1. The *F. vulgare* plant sample and experimental animal.

Figure 2. Effect of fine powder of *F. vulgare* on serum biomarkers ethanol (30%) intoxicated male rats.

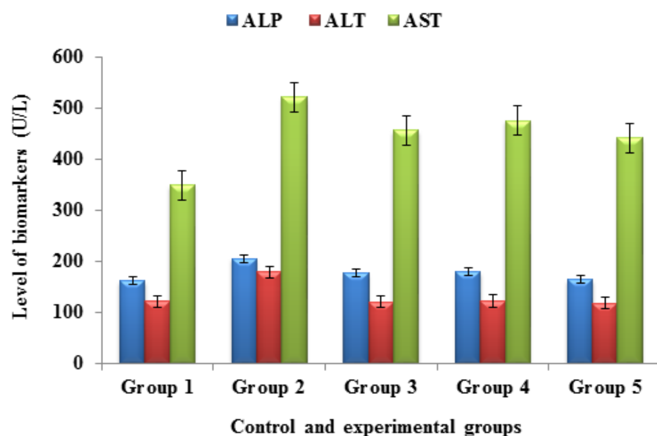
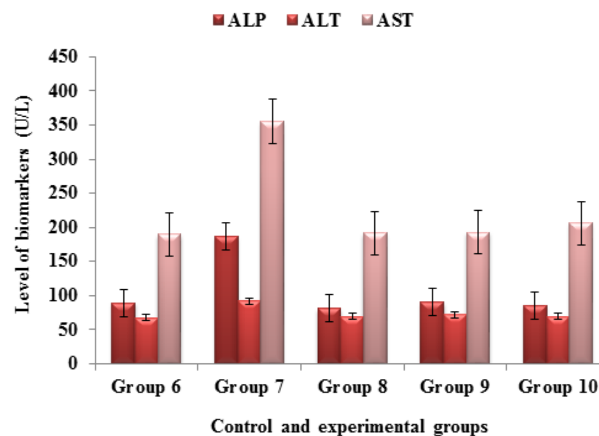


Figure 3. Effect of fine powder of *F. vulgare* on serum biomarkers ethanol (30%) intoxicated female rats.



DISCUSSION

The present study has been attempted to demonstrate the hepatoprotective effect of *F. vulgare* in 30% of ethanol intoxicated male and female albino rats. The presence of higher concentration of secondary metabolites like flavonoids and terpenes in the *F. vulgare* indicates that it is an effective hepatoprotective agent. The presence of essential micronutrients like calcium and magnesium concentration is higher followed by other micronutrients such as copper, zinc and iron with the least levels of cadmium come to an end that the leaves are nontoxic and safe to be included in tea, beverages and food soups as a garnishing agent.

The reduction in body weight of alcohol intoxicated male and rats denotes that excess of alcohol consumption will be the source of liver disease by interfering with the nutritional intake, absorption and utilization of various nutrients in the body. Additionally, alcohol exerts some harmful effects through metabolism which results in the generation of toxic compounds, particularly in the liver [39]. The decrease in the body weight of male (Group 2) and female (Group 7) alcohol intoxicated groups confirmed the liver damage and the inability of rats to utilize the feed and water because of stress induced by alcohol. The moderate increase in body weight of male and female rats compared to control groups after treatment with two different doses of *F. vulgare* inherent its cell regeneration capacity and its cytoprotective effect. Silymarin is a well-known hepatoprotectant, whose data's are near to the values of drug treated rat's confirmed the protective effect of the *F. vulgare*.

The wet weight of the hepatocytes isolated from alcohol intoxicated groups in males (Group 2) and females (Group 7) were increased compared to control males (Group 1) and females (Group 6). This is due to the chemically reactive nature of acetaldehyde which form irreversible adducts in the structural and microsomal proteins and increases the lipid peroxidation in liver cells. This leads to the accumulation of fat in the liver by increasing the liver mass with the appearance of swollen mitochondria inside the liver cells. The results intimate that *F. vulgare* is a good hepatoprotective agent in reducing the fat accumulation in the liver and its regeneration capacity was inherent by the values of drug treated rats near to the control groups.

ALT and AST were used as diagnostic enzymes in identification of alcoholic liver disease. The ALT is more specific than AST for alcohol related liver injuries because this enzyme is found predominantly in the liver**.** The elevated levels of ALT and AST in the present investigation confirmed that alcohol damaged the liver cells. The distortion in the liver lead to the leakage of marker enzymes into the blood stream that is observed as high ALT and AST in alcohol intoxicated groups compared to control rats. Our findings are supported by other research

work conducted in human volunteers with a rapid increase in ALP, ALT and AST [40].

The treatment of *F. vulgare* in male and female rats simultaneously reduced the leakage of ALT and AST by indirectly regenerating the liver cells. The results manifested that *F. vulgare* acts as good hepatoprotectant in stabilizing the liver distortion and regenerate the liver cells by the stimulatory effect of flavonoids present in fennel. Our results are supported by other research carried out in aqueous extract of *curcuma longa* that decreased the ALP, AST and ALT in ethanol intoxicated albino rats [41].

The increase concentration of bilirubin in serum is a signal of hyperbilirubinemia in alcohol intoxicated groups. The excess production of total bilirubin observed in the present study might be the cause of rapid turnover in the catabolism of heme and in the increased concentration of unconjugated bilirubin. In addition the alcohol expresses the structural and functional damage in the liver which was unable to precede the conjugation reactions and to detoxify the xenobiotics.

Rats treated with 50 mg/kg of *F. vulgare* and 1 g/kg of *F. vulgare* in males (Group 4 – Group 5) and females (Group 9 – Group 10) treated groups decreased the concentration of total, direct and indirect bilirubin compared to Silymarin treated groups. The significant reduction of total bilirubin observed in the present study is in consistent with other research report conducted on the hepatoprotective effect of picroliv in ethanol fed albino rats [42].

The reduction in total proteins, albumin and globulin in alcohol intoxicated groups might be the sparing effect of the tissue proteins in the synthesis of immunoglobulins / antibodies. The decrease in concentration of proteins is a strong evidence for the stress induced by alcohol. Total proteins might be used to control the formation of reactive acetaldehyde and to regulate the oxidation reactions rather than influencing the anabolic reactions in cells. On a whole these serum proteins may act as primary defensive scavengers to protect the potential organs from the vulnerable damage induced by the alcohol. Albino rats treated with *F. vulgare* confirmed the hepatostimulatory effect of *F. vulgare* by increasing the concentration of serum proteins which is important for the functions of liver cells. The increased concentration of total proteins, albumin and globulin after treated with *F. vulgare* is in agreement with the research carried out in hepatoprotective effect of *Tagetes erecta* in ethanol intoxicated rats [43].

CONCLUSION

The present research work demonstrated the hepatoprotective effect of leaves of *F. vulgare* in alcohol induced male and female albino rats as in vivo model. The results of the present study registered the ALP, ALT and AST were stabilized on treatment with *F. vulgare*. Fennel leaves significantly increased the concentration of total proteins, albumin and globulin and decreased the concentration of bilirubin in alcohol intoxicated male and female rats. This concluded the present medicinal plant *F. vulgare* is a potent hepatoprotectant. All biochemical parameters are similar in their trend and no significant changes were observed in the male and female albino rats. The two doses of *F. vulgare* (50 mg/kg.b.wt and 1 g/kg b.wt) showed similar effect in males and females compared to Silymarin and control groups. The optimum dose of 1 g/kg b.wt recorded the results similar to the control groups. The present study was a pilot trial and however more work has to be carried out to identify, isolate and quantify the phytochemical compound responsible for this curative effect. As a final stage of recommendation, it is must to conserve *F. vulgare* and more future research work should be carried out in this plant to explore its different protective effect against different diseases.

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