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Original Article

Comparative and Combined Effects of *Echium amoenum* and *Cichorium intybus* Extracts on the Live of Wista Rats

Monireh Ranjbar[1*] and Nilufar Motiee[2]

[1]*Department of Biology, Falavarjan Branch, Islamic Azad University, Isfahan, Iran*
[2]*Department of Biochemistry, Falavarjan Branch, Islamic Azad University, Isfahan, Iran*

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***Corresponding author**
ranjbar@iaufala.ac.ir

ABSTRACT

The study is aimed to evaluate the effects of *Echium amoenum* Fisch. & C.A.Mey. and *Cichorium intybus* L. extracts on the liver of Wistar rats. Ninty rats were divided into 15 groups. Group 1 received physiological serum, groups 2, 3, 4 and 5 40 mg/Kg, 6, 7, 8 and 9, 400 mg/Kg, 10, 11, 12 and 13, 1000 mg/Kg aqueous and ethanolic extract of *C.intybus* and *E. amoenum*, group 14 and 15, 400 mg/Kg combined aqueous and ethanolic extracts. Blood samples were collected to assay AST, ALT, ALP, GGT, MDA, total protein and bilirubin levels. The effect of different concentrations of aqueous extracts of Chicory and Echium on AST, ALT, ALP, GGT and bilirubin levels is the same. Concentrations of 40 to 1000 mg/kg of Chicory ethanol extract had different effects on AST, ALP and bilirubin, but in the case of ALT, the differences were between 40 and 400 mg/kg. The flavonoid and anthocyanin contents were the highest in ethanolic extract of Echium. Antioxidant activity and total phenols content in ethanolic extract were higher than aqueous extract. The use of aqueous extract of Chicory in high concentrations did not harm the liver. Ethanolic extracts of both plants at 1000 mg/Kg will damage the liver. The ethanolic extracts of both plants contain many phenolic compounds that increase the inhibition of free radicals in this extract.

INTRODUCTION

In traditional medicine, medicinal plants are widely used for the treatment of various diseases, but the effects of biologically active compounds of some plant species on human health are unknown [1]. Medicinal plants contain active ingredients in one or more of their organs. These substances, which constitute less than ٪1 dry weight of the plant, have medicinal properties affecting living organisms [2]. *Echium amoenum* is an annual, dicotyledonous plant belonging to the Boraginaceae family. *E. amoenum* grows in the northern regions of Iran and parts of Europe. The flowers and leaves of this medicinal plant are useful to treat stress and depression. This plant is widely used in medicine due to its potassium nitrate and anti-inflammatory effects [3]. Experiments have shown that flowers of Iranian borage contains some alkaloids, tannins and cyanogenic glycosides, and have different amounts of flavonoids, Saponins and unsaturated Sterols. In western spices of this herb, the presence of pyrrolizidine alkaloids, echinone and echinofuran have been reported [4]. *Cichorium intybus* is a wild, perennial herbaceous plant with a height of 0.5 to 1.5 meters. *C. intybus* treats liver disease. It has antioxidant properties because t is a rich resource of phenolic compounds, vitamins A, C, as well as potassium, calcium, and phosphorus. All parts of the herb, especially its roots and leaves, have a tonic effect on the stomach, are diuretic, blood purifier, laxative, biliary, and antipyretic [5].

In order to investigate the toxic effect of *E. amoneum*, Abbasi *et al*. brewed it and gavaged it to rats at concentrations of 40, 400 and 800 mg/kg. They found no significant difference in the levels of liver enzymes including ALT and AST, and the extract infusion of this plant in the mentioned doses had no toxic effect on the liver [6]. Chicory extract has been reported to decrease bilirubin levels under in vitro conditions [7]. Ghorbani *et al*. investigated the toxic effects of methanolic extract of *E. amoneum*. They injected extract of this plant in

doses of 100 and 200 mg/kg to mices and concluded that the level of liver enzymes in these two groups was significantly more than the control group therefore this plant is responsible for hepatotoxicity [8]. Chicory is used for the treatment of AIDS, cancer and diabetes, because of its anti-radical and antioxidant compounds in the root [9]. Hassan *et al*. (2010), showed that the methanolic extract of *C. intybus* seeds may have reduced the cytotoxicity of bleomycin on non-malignant skin cells by its antioxidant effect, while it did not have such a protective effect on ovarian cancer cells. Furthermore, they showed that in Indian medicine, *C. intybus* seed is used to treat liver disease and diarrhea. Methanolic fraction of Chicory seeds has protective effect against hepatotoxicity induced by carbon tetrachloride. *C. intybus* seeds have a high amount of polyphenolic compounds, especially caffeoylquinic acids derivatives [10]. Chicory leaves have anthocyanins, vitamins A and C, which stimulates the immune system and control infection and inflammation, also, the use of Chicory reduces liver toxicity caused by nitrosamine and increases resistance to oxidative stress [11]. According to previous research, studying the effect of Echium and Chicory extracts concentration on liver is required.

MATERIALS AND METHODS

Ethical Approval

Animals were handled according to the guidelines set by the National Research Council of the National Academies for the care and use of laboratory animals [12].

Experimental Animals

In this study, 90 Wistar rats with an average weight of 200-250 g were prepared from Falavarjan Azad University (Code of Ethics IR.IAU.NAJAFABAD.REC.1398.074). Rats were randomly divided into 15 groups. For animal adaptation to nesting environment under standard conditions, they were allowed free access to food and water for a week before experimentation.

Plant Collection and Extraction

Fresh *E. amoneum* (herbarium code: 104/011/001) and *C. intybus* (herbarium code: 124/101/001) were prepared from Isfahan Agricultural Research Center. The following steps have been performed for the preparation of the plant ethanolic and aqueous extracts. 50 g of dry powder of each plant was poured into a 1000 ml Erlenmeyer flask and mixed with 500 ml of 80% ethanol, the Erlenmeyer lid was closed with foil, and then the extraction was performed on a shaker. After 72 hours of extraction, the solution was filtered. The ethanolic extract was concentrated by a rotary evaporator at 45 °C and then dried. To prepare the aqueous extract, 500 ml of sterile distilled water was mixed with 50 g of stem and leaf powder and boiled for 20 minutes. After passing through a strainer, the extract was dried. Group 1 received physiological serum, groups 2 and 3, 40 mg/Kg aqueous and ethanolic extract of *C.intybus*, 4 and 5 40 mg/Kg aqueous and ethanolic extract of *E. amoenum*, groups 6 and 7, 400 mg/Kg aqueous and ethanolic extract of *C.intybus*, 8 and 9, 400 mg/Kg aqueous and ethanolic extract of *E. amoenum*, groups 10 and 11, 1000 mg/Kg aqueous and ethanolic extract of *C.intybus*, 12 and 13, 1000 mg/Kg aqueous and ethanolic extract of *E. amoenum*, group 14, 400 mg/Kg aqueous extract of *C.intybus* and *E. amoenum* and group 15, 400 mg/Kg ethanolic extract of *C.intybus* and *E. amoenum*. In the present study, groups 10 and 15 were excluded during the experiment, because of their mortality. Aqueous and ethanolic extracts of Echium and Chicory plants were gavaged at concentrations of 40, 400 and 1000 mg/kg every day at certain times; after 30 days, blood samples were taken from all tested groups and serum levels of AST, ALP, ALT, GGT, MDA, total bilirubin were determined.

Determination of Phenolic Contents

The total phenolic content was determined for individual extracts using the Folin–Ciocalteu method. Briefly, 1 mL of extract (100–500 µg/mL) solution was mixed with 2.5 mL of 10% (w/v) Folin–Ciocalteu reagent. After 5 min, 2.0 mL of Na_2CO_3 (75%) was subsequently added to the mixture and incubated at 50 °C for 10 min with intermittent agitation. Afterward, the sample was cooled and the absorbance was measured utilizing a UV Spectrophotometer (Shimazu, UV-1800) at 765 nm against a blank without extract. The outcome data were expressed as mg/g of gallic acid equivalents in milligrams per gram (mg GAE/g) of dry extract [13].

Determination of Flavonoid Contents

An aliquot of 1 mL of extract solution (25–200 µg/mL) or quercetin (25–200 µg/mL) were mixed with 0.2 mL of 10% (w/v) AlCl3 solution in

methanol, 0.2 mL (1 M) potassium acetate and 5.6 mL distilled water. The mixture was incubated for 30 min at room temperature followed with the measurement of absorbance at 415 nm against the blank. The outcome data were expressed as mg/g of quercetin equivalents in milligrams per gram (mg QE/g) of dry extract [13].

Determination of Total Anthocyanin Content

The total anthocyanin content was determined by the pH differential method which bases on the structural changes in chemical forms of anthocyanin and absorbance measurements at pH 1.0 and 4.5. Crude extracts were diluted separately with 0.025 M hydrochloric acid potassium chloride buffer (Ph = 1) and 0.4M sodium acetate buffer (Ph = 4.5). Each sample was diluted with the buffers to give an absorbance reading between 0.2 and 1.4. The absorbance of the mixture was measured at λvis-max and 700 nm using a UV-Vis spectrophotometer (UV1601; Shimadzu, Kyoto, Japan). The total anthocyanin content was expressed as cyanidin-3-glucoside equivalents as in the following equation.

Anthocyanin pigment (mg/L) = A ×MW ×DF ×V ×1000 /a ×l ×m (1)

where A is the absorbance, MW is the molecular weight of cyanidin-3-glucosode (449.2 g/mol), DF is the dilution factor, V is the solvent volume (mL), a is the molar absorptivity (26,900 L.mol−1.cm−1), and l is the cell path length (1 cm) [14].

DPPH Radical Scavenging Activity

The radical scavenging activity (RSA) of the crude extracts was adopted to measure antioxidant activity using the DPPH method. Briefly, 2 mL of extract solution (1–100 µg/mL) in methanol was added to 2 mL of DPPH (0.1 mM) solution. The mixtures were kept aside in a dark area for 30 min and absorbance was measured at λ max 517 nm against an equal amount of DPPH and methanol as a blank. The percentage of DPPH• scavenging (RSA %) was estimated using the equation: % scavenging of DPPH• = [(A0 − A1)/A0] × 100, (1)

Where A0 = absorbance of the control and A1 = absorbance of the test extracts [12].

Statistical Analysis

SPSS 21 software, one-way analysis of variance (One Way ANOVA) and post hoc test (LSD) were used for statistical analysis. Furthermore, a significance level of less than 0.05 was considered for all analyzes.

RESULTS AND DISCUSSION

Phenol and Flavonoid Contents

The purpose of the current study was to investigate the comparative and combined effect of Echium and Chicory extracts on the liver of Wistar rats. In the present study, changes in serum levels of ALT, AST and ALP enzymes also GGT, MDA, total bilirubin were evaluated as an indicator of liver damage. Antioxidant capacity, Phenol, flavonoids and anthocyanins contents of Echium and Chicory extracts were determined, and the results of other researchers were compared with the results of the present study.

The content of total phenols in aqueous and hydroalcoholic extracts of Echium and Chicory is shown in figure 1. Ethanolic extract of both plants had the highest amount of total phenols. The lowest amount of total phenol was in the aqueous extract of Chicory. The ethanolic extract of both plants had more total phenol than the aqueous extract.

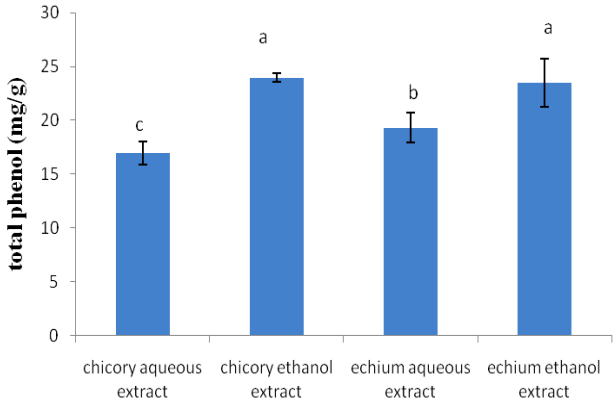

Fig. 1 Comparison of total phenols content of aqueous and hydroalcoholic extracts of *E. amoneum* and *C. intybus*. Dissimilar letters indicate significant differences ($p< 0.05$) between groups

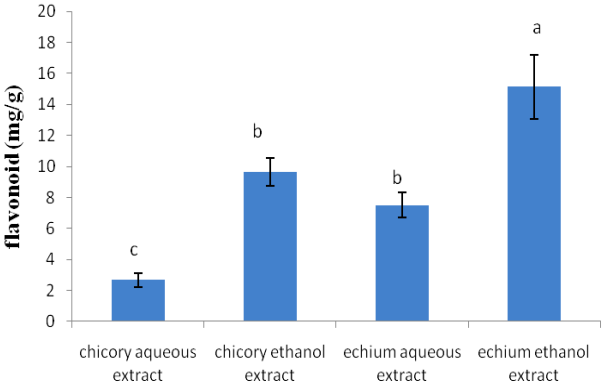

Fig. 2 Comparison of flavonoids content of aqueous and hydroalcoholic extracts of *E. amoneum* and *C. intybus*. Dissimilar letters indicate significant differences ($p< 0.05$) between groups

Figure 2 shows the flavonoids content of aqueous and hydroalcoholic extracts of *E. amoneum* and *C. intybus*. The highest and lowest levels of flavonoids were in the ethanolic extract of Echium and Chicory extract, respectively. The ethanolic extract of both plants had more total phenol than the aqueous extract.

Hydroalcoholic solvents are preferred for the extraction of polar antioxidant compounds because the glycosidic and polar phenols and flavonoids compounds are well soluble in this solvent. These compounds play an important role in the antioxidant properties of plants. Phenolic and flavonoid compounds usually bind to one or more sugar molecules, in which case their solubility increases. Identification of components in aqueous extracts can reveal the type of antioxidant compounds isolated. The compounds in this extract are very hydrophilic [15]. Flavons and their glycosidic derivatives in hydrophilic solutions have higher antioxidant properties than hydrophobic. In the polar environment, they are often in the form of ions with acidic properties that are more stable than water hydroxyl ions. The stability of resonance structures of these compounds plays an important role in their antioxidant properties. The yellow aqueous extracts can also be due to the presence of water-soluble carotenoids, which are usually potent antioxidants. Such as aqueous extracts of saffron, which contain a variety of water-soluble crocins and have high antioxidant properties [16]. According to the results of the present study, the content of phenolic compounds in ethanolic extract of *C. intybus* and *E. amoneum* was higher compared to aqueous extract, which shows that the type of solvent directly affects the extraction of phenolic compounds.

Antioxidant Activity

The level of antioxidant activity and comparison of 50% of free radical scavenging in aqueous and hydroalcoholic extracts of Echium and Chicory are shown in figures 3 and 4. Antioxidant capacity results in aqueous and ethanolic extracts of *C. intybus* and *E. amoneum* indicates that the alcoholic extract of *E. amoneum* was able to inhibit the highest level of free radicals, which is probably due to the high content of total phenols in this extract. Chicory aqueous extract had the lowest percentage of free radical scavenging, which was consistent with low levels of total phenols in it. Alcoholic extract of chicory had a higher percentage of free radical scavenging than aqueous extract. There was a similar result in *E. amoneum*. The IC50 results of the ethanolic extract of Chicory and Echium indicated that the aqueous extract of *C. intybus* requires a higher concentration to inhibit 50% of free radicals, but the alcoholic extract of Echium at much lower concentrations can inhibit the same number of free radicals. Alcoholic extracts of both plants inhibit half of the free radicals at lower concentrations of aqueous extracts. Hashemi *et al* in 2019 determined the total phenol and flavonoid content and antioxidant capacity of ethanolic extract of Echium shoot and showed that the extracts of shoots of *E. amoneum* had a high total phenol and flavonoid contents [17].

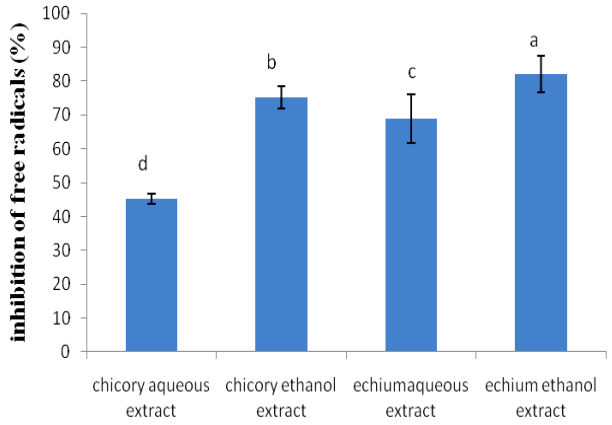

Fig. 3 Comparison of antioxidant activity of aqueous and hydroalcoholic extracts of *E. amoneum* and *C. intybus*. Dissimilar letters indicate significant differences ($p<0.05$) between groups.

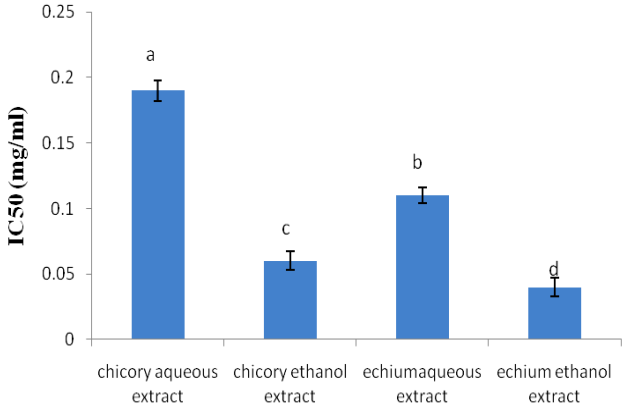

Fig. 4 Comparison of 50% free radical scavenging in aqueous and hydroalcoholic extracts of *E. amoneum* and *C. intybus*. Dissimilar letters indicate significant differences ($p< 0.05$) between groups.

According to the IC50, the antioxidant capacity of the ethanolic extract of Echium was lower than

ascorbic acid and quercetin and plants such as *Achillea millefolium* and *Hypericum perforatum*, and higher than Lamium [18]. Due to the fact that the DPPH method was used to determine the antioxidant capacity and water was used as a solvent in this method, polar extracts had a higher antioxidant capacity. Therefore, DPPH method is more suitable for determining the antioxidant capacity of hydrophilic compounds. The lower the IC50, the greater the antioxidant capacity of the extract because the extract with less concentration inhibits more free radicals [19]. The antioxidant capacity of various extracts of *Dracocephalum Kotschyi* and the amount of total phenols and flavonoids are directly related. Increasing the concentration of the extract increases the antioxidant capacity. In the present study, the ethanolic extract had the lowest IC50 and the highest antioxidant capacity, which is consistent with the intended results. Moradi also suggested that the ethanolic extract of Dracocephalum kotschyi with high antioxidant capacity could be a good alternative to synthetic antioxidants BHT [20].

Anthocyanin Content

Figure 5 shows the amounts of anthocyanins in aqueous and hydroalcoholic extracts of Echium and Chicory. The alcoholic extract of *E. amoneum* and *C. intybus* had the highest level of anthocyanin. The lowest level of anthocyanin was observed in the aqueous extract of *E. amoneum*.

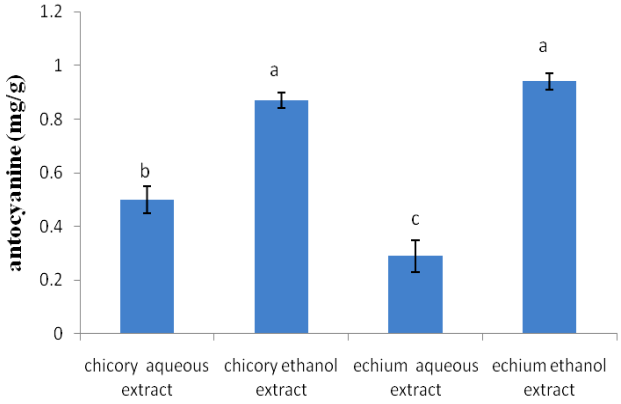

Fig. 5 Comparison of anthocyanin content of aqueous and hydroalcoholic extracts of *E. amoneum* and *C. intybus*. Dissimilar letters indicate significant differences ($p< 0.05$) between groups

One of the most important phytochemicals of echium is anthocyanin, which is present in this plant with saponin and other phenolic compounds [21].

Biochemical Studies

Table 1 shows the activity of enzyme AST, ALT, ALP, and the levels of Tbili, Tpro, GGT, MDA. The results of AST, ALT and ALP in the groups aqueous and ethanolic extracts of Chicory and Echium showed that AST, ALT and ALP levels in none of the concentrations of *C. intybus* aqueous extract were significantly different from the control, but AST and ALT enzymes in the group receiving 1000 mg/kg aqueous extract of *E. amoneum* was increased compared to the control. The levels of AST, ALT and ALP enzymes had increased with increasing concentrations of ethanolic extract of *E. amoneum*. The mean amount of total protein in all groups except the group receiving the aqueous extract of Echium was not significantly different from the control group. Total bilirubin level in the 1000 mg/kg ethanolic extract of Echium was increased compared to the control group. There was no significant difference in bilirubin level between different groups of Chicory aqueous extract. The amounts of bilirubin in the alcoholic extract groups of Chicory and the combined group of Chicory and Echium extract at 400 mg/kg were different from the control. The amount of bilirubin in the group of Echium aqueous extract was different at concentrations of 1000 and 40 mg/kg. Bilirubin levels were different in the 40 and 1000 mg/Kg alcoholic extract of Echium. There was a significant increase in the amount of gamma glutamyl transferase in the groups receiving 400 and 1000 mg/kg ethanolic extract of Echium compared to the control group. No significant difference was observed between different groups of aqueous and alcoholic extracts of *C. intybus* in terms of GGT content. The amount of GGT in the group of the aqueous extract with a concentration of 40 mg/kg was different from the group of 1000. The amount of GGT was different in the three concentrations of the alcoholic extract of Echium. The mean level of gamma glutamyl transferase in the groups receiving 400 and 1000 mg/kg ethanolic extracts of Echium was significantly increased compared to the control group. The amount of GGT did not differ between the different groups receiving aqueous and alcoholic extracts of C. intybus. In the aqueous extract group, the 40 mg/kg group was different from the other groups by 1000 mg/kg. The amount of GGT in the groups receiving three concentrations of alcohol extract was different from each other.

Table 1 Comparing the effect of aqueous and hydroalcoholic extracts of *E. amoneum* and *C. intybus* on AST, ALT, ALP enzyme functions, and the amount of Tbili, Tpro, GGT, MDA

	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	Tbili (mg/dl)	Tpro (mg/dl)	GGT (mg/dl)	MDA (mg/dl)
Control	72.33±0.57 *	40.33±0.57 *	165±14.17 *	0.44±0.026 *	6.33±0.49	3.96±0.73*	4.75±0.50*
Chicory aqueous extract 40 mg/kg	53.16±6.05 *	20.73±2.23 *■	217.66±37.70	0.46±0.06	6.35±0.52	3.32±0.76	3.97±0.39O
Chicory ethanolic extract 40 mg/kg	57.25±6.06 *■	20.36±3.40 *	192.83±26.73 ■	0.386±0.04 ■	6.783±0.9	4.10±0.75	5.23±0.51
Echium aqueous extract 40 mg/kg	49.5±3.61*♯	12.08±1.90*&	211.75±16.20	0/4883±0.05 ♯	5.67±0.66 ♯	4.85±0.26 ♯	5.11±0.38
Echium ethanolic extract 40 mg/kg	65.33±8.38 &	24.43±4.04 *	206.5±39.54&	0.45±0.03	6.78±0.37	2.34±0.80 &	5.37±0.42
Chicory aqueous extract 400 mg/kg	64.3±6.24	18.36±2.88 *■	204.3±10.91	0.41±0.06	6.34±0.89	3.64±0.81	5.27±0.58O
Chicory ethanolic extract 400 mg/kg	65.25±4.63	15.71±2.92 *	208±33.05	0.38±0.07	6.08±0.37	3.41±0.8	5.54±0.55
Echium aqueous extract 400 mg/kg	63.25±3.18	23.25±0.35 *&	270±1.41*	0.50±0.02	5.90±0.28♯	4.50±0.64	4.94±0.64
Echium ethanolic extract 400 mg/kg	75.08±7.34 &	25.91±2.08 *	305.16±44.47*&	0.41±0.05	6.78±0.78	6.60±0.90 &	5.24±0.37
Chicory ethanolic extract 1000 mg/kg	72.2±5.40 ■	21.26±3.74 *	296.4±26.68 *■	0.49±0.05 ■	612±035	3. 64±0.55	5.24±0.31
Echium aqueous extract 1000 mg/kg	94.4±0.56 *♯	37.25±0.35	271±1.41*	0.55±0.007 ♯	6.65±0.21♯	6.4±0.28 ♯	60.5±0.06 *
Echium ethanolic extract 1000 mg/kg	71.25±5.89 &	25.05±2.14 *&	276.33±29.12*&	0.62±0.06 *&	6.93±0.26	6.94±0.98 *&	5.44±0.67
Chicory Echium ethanolic extracts 400 mg/kg	74±6.71■	18.6±3.93 *	257±29.53 *	0.518±0.06 ■	6.08±0.70	4.15±0.92	5.30±0.65

AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; ALP: Alkaline Phosphatase; Tbili: Total Bilirubin; Tpro: Total Proteins; GGT: Gamma-Glutamil Tranferase; MDA: Malondialdehyde
* shows a significant difference between the control group and other groups, O Shows significant differences in different concentrations of aqueous extract of chicory, ■ Shows significant differences in different concentrations of ethanolic extract of Chicory, ♯ Shows significant differences in different concentrations of aqueous extract of Echium, & Shows significant differences in different concentrations of ethanolic extract of Echium

Li *et al*. (2014)investigated the effects of Chicory hydroalcoholic extract on carbon tetrachloride-induced liver fibrosis. They reported this extract protected the liver against carbon tetrachloride fibrosis by reducing the amount of malondialdehyde and increasing the activity of hepatic superoxide dismutase. They also suggested that serum levels of AST and ALT were reduced by treatment with Chicory extract. In the present study, one of the mechanisms involved in the protection of the liver by *C. intybus* may be the presence of antioxidant compounds. The amount of malondialdehyde in the group receiving a concentration of 1000 mg/kg of Chicory aqueous extract was higher than in other groups. At this concentration, a significant increase was observed compared to the control group. Therefore, this concentration of Chicory extract causes damage to cell membranes and liver [22].

Seven days of consumption of 800 mg/kg Chicory root extract in rats with liver damage, reduced the levels of liver enzymes ALT and AST. Chicory extracts due to its high antioxidant capacity stabilize the cell membrane of the liver and prevent damage to it. Therefore, it reduces the level of ALT and AST in the blood [23]. Effects of *C. intybus* on male rats with liver disease were investigated. Eight weeks of consumption of Chicory extract could reduce AST and ALT enzymes [24]. The antioxidant effects of *C. intybus* may be due to the presence of polyphenolic compounds in this plant that act as electron donors and prevent oxidation [25]. The researchers suggested that Chicory extract, as a natural antioxidant, protects the liver but needs further research. 100 mg/kg of *E. amoneum* extract does not increase AST and ALT enzymes, so there is no hepatotoxicity at this concentration, but a concentration of 200 mg/kg of this extract damaged the liver and increased AST and ALT. In the present study, AST and ALT levels increased with increasing aqueous extract concentration, which is consistent with the study of Abbasi *et al*. [26]. In the present study, ethanolic extract of echium with a concentration of 400 mg/kg caused liver damage. In fatty liver rats, consumption of the echium extract at a concentration of 200 mg modulated liver biochemical markers. Histological studies also showed that a high-fat diet causes fat storage in liver cells and the accumulation of inflammatory cells in the liver. However, receiving a concentration of 200 mg of the extract reduces steatosis in liver cells and improves inflammation in liver tissue.

But, the concentration of 400 mg of the combined extract had no significant effect on liver tissue [27].

Giannini *et al*. (2005) showed that ALT, AST, and GGT activity is good indicator for determining liver function. These enzymes are produced in the cytosol of liver cells, and when the liver cells are damaged, these enzymes are released into the blood plasma, and their activity in the plasma increase [28]. As a result of damage to the liver cells, the cell membrane is destroyed and its enzymes enter the bloodstream, and their concentration in the serum increase [28]. In the present study, GGT increased in the groups receiving ethanol extract 1000 and 400 mg/kg and in the groups receiving an aqueous extract of Echium 40 and 1000 mg/kg. According to the results of Ghorbani *et al*., long-term consumption of Echium extract causes liver damage and increases the amount of GGT enzyme. GGT enzyme was lower in the group receiving 40 mg/kg of Echium ethanol extract compared to other concentrations of Echium ethanolic extract. Ethanol extract at this concentration did not cause liver damage and did not increase GGT enzyme [8].

The effect of Chicory fruit extract on the reduction of total and direct bilirubin in the group receiving 100 mg/kg of Chicory extract compared to the control group has been reported. One of the causes of liver damage in biliary obstruction is an increase in bile acids and a change in the balance of antioxidant compounds, which leads to various complications by stimulating fat peroxidation. In addition, oxidative stress is usually increased in cirrhosis [29]. Some studies have reported the effect of antioxidant compounds such as vitamins C and E in improving cholestasis [23]. Chicory leaf extract contains large numbers of anthocyanins, vitamins A and C, which limit inflammation [21]. Probably part of the effects of Chicory extract on inflammatory and liver damage markers was due to these compounds. Moreover, Chicory extract has been reported to decrease bilirubin levels under in vitro conditions [29].

CONCLUSION

Although the alcoholic extract of beetle flower had high phenol, flavonoids and anthocyanins and inhibited a high percentage of free radicals in the environment, but in high concentrations did not have a positive effect on liver activity.

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