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Review Article

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Hepatoprotective Essential Oils: A Review

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Objectives: Several toxins and molecules are able to damage the liver, causing the hepato-toxicity. This disorder can be protected naturally, by some essential oils obtained from different plants. In this review we are cited some of these compounds that have been tested by their hepatoprotective effect.

Methods: We reviewed 83 articles published between 1981 and 2018 in English via three databases Sciencedirect, Springer and PubMed. So, we have used the keywords: Hepatoprotective effect, liver disease, plants and essential oils.

Results and conclusion: In this work, we classified the plants; contain the essential oils, in alphabetical order as a table containing the scientific, family names, information plants, the experimental assay and the results obtained from the hepatoprotective studies. We have described 27 species belonging to 12 families: Lamiaceae (7 species), Asteraceae (6 species), Umbellifereae (3 species), Apiaceae (3 species) are the main families which enclose the species that was studied. The study also includes the major compounds isolated from some of these essential oils. The most of those compounds belong to terpene class essentially cineol, carvacrol and thymol. Thus, the different essential oils that have been cited in this review were shown that have an antioxidant activity.

Keywords: hepatoprotective effect, essential oils, medicinal plants, hepatotoxic agents

INTRODUCTION

Essential oils are natural compounds obtained from aromatic herbs and characterized by a strong smell. They are volatile and complex components, mostly obtained by hydro-distillation or steam method that was developed by Arabs in the middle ages. Currently, there are 300 essential oils commercially in different applications: Pharmaceutical, cosmetic, perfume, agronomic and food [1]. They have been used for their beneficial properties such as insecticidal, [2] antibacterial [3] and antifungal activities [4].

Some essential plant oils are used to treat and manage different diseases as well as the liver damages. Indeed, many researches were done on certain of these oils, reported that these components have a hepatoprotective action. So, in this paper, we have cited some of these essential oils, referencing back to the various works that have been published in three databases: Sciencedirect, Springer and PubMed.

MATERIALS AND METHODS

In this paper, we included 83 works published between 1981 and 2018 in English, collected from Sciencedirect, Springer and PubMed databases. To find these publications, we have used the following keywords: Hepatoprotective effect/activity, liver disease, plants and essential oils. Therefore, 23 articles based on experimental studies of some plant essential oils against hepatotoxicity actions were included in this review.

RESULTS

In the present work, we classified the plants in the form of the table (Table 1) contains the scientific, family names, plants information and even the experimental assay and the results obtained from the hepatoprotective studies.

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Table 1. Hepatoprotective essential oils

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Achillea biebersteinii Afan	Asteraceae	The countries around the Mediterranean Sea and the Arabian Peninsula are the native origin of *A. biebersteinii*, which is a perennial plant, characterized by 30 to 60 cm in high. This herb used traditionally to treat abdominal pain, wound healing and liver diseases like jaundice.	The protective effect of the essential oil obtained from the aerial parts of *A. biebersteinii* has been evaluated; using carbon tetra-chloride (CCl_4) at a dose of 1.25 mL/kg induced hepatotoxicity in Wistar albino rats. Then, the liver was dissected to perform the biochemical and histological examination. The results showed that the administration of the essential oils at a dose of 0,2 mL/kg has a significant hepatoprotective activity against CCl_4 induced liver damage compared with control. Furthermore, the biochemical assay indicated that this oil contains: 56.3% of the monoterpene hydrocarbons, 29.2% of the monoterpene hydrocarbons alfa-terpinene, 22.9% p-cymene, 4.7% terpinen-4-ol, 4.3% of 1,8-cineole, 3.9% of trans-p-menth-2-en-1-ol, 3.1% of the ascaridole, 2.5% of trans-piperitone oxide and 2.1% carvacrol [7].	Monoterpene hydrocarbons, α-terpinene, *p*-cymene, oxygenated monoterpenes of the total oil, terpinen-4-ol, 1,8- cineole, trans-*p*-menth-2-en-1-ol, ascaridole, trans-piperitone oxide and carvacrol (7)
Achillea wilhelmsii	Asteraceae	*A. wilhelmsii* used extensively in Iran as a medicinal herb to treat a lot of health problems. It has an anti-oxidant, anti-microbial, anti-hypertensive, anti-hyperlipidemia and immunomodulatory effects [8-11]	The hepatoprotective activity of the essential oils obtained from the aerial parts of this plant was evaluated on acetaminophen induced liver disorders in Wistar rats, "by increasing of oxidative stress and free radicals". Five hundred mg/kg of the acetaminophen and the essential oils at two different doses (100 and 200 mg/kg) were injected intraperitoneally in animals. Then, superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), the ferric reducing ability of plasma (FRAP), and lipid peroxidation (LPO) parameters were measured after the treatment in 2, 4, 8, 16 and 24 hours. The experiment results showed that acetaminophen treatments increased the levels of SOD, LPO, and FRAP with the diminishing of GSH level. Furthermore, the treatment with *A. wilhelmsii* oils at doses 100 and 200 mg/kg with acetaminophen restored significantly the GSH and reduced the rise of SOD, LPO, and FRAP levels as compared with the control. To confirm the finding results, the histo-phatological examination was carried out by using small portions of the liver that showed the presence of the hepatic necrosis inhibited by the essential oils [12].	*p*-ocimen, 1,8 cineole, carvone, camphor, and verbanol acetate (13).

Table 1. Continued 1

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Ajuga iva	Lamiaceae	*A. iva* is an annual herbaceous herb. It has several beneficial effects, particularly in gastrointestinal problems, hypertension and diabetes [13].	The essential oils obtained from the air-dried aerial parts of this plant were evaluated by their hepatoprotective effect at a dose of 50 mg/kg body weight on 5 mL/kg of CCl_4 inducing liver damage. The tested oil was administered every day for two weeks before the injection of CCl_4 "intraperitoneally". Then, the chemical composition of *A. iva* oils was defined by gas chromatography associated to mass spectrometry "GC-MS". The results of the experiment indicated that the essential oil of *A. iva* possesses a hepatoprotective activity which may be explicated by their antioxydant activity. Besides, there are 48 compounds that were identified in this plant, representing 99.40% of the total oil profile, with 35.07% of carvacrol [14].	1,8- Cineole, linalool, camphor, borneol, terpinene-4-ol, methyl chavicol, carvone, carvotanaceton, Z- anethol, thymol, carvacrol, trans-carvyl acetate (15).
Anethum graveolens L.	Apiaceae	*A. graveolens L.* is an annual plant that used traditionally to treat different diseases and it is used too, as a condiment. South-eastern Europe and Mediterranean countries are the native land of this plant [15]. Moreover, it has been declared by Heamalatha and al in 2011 that *A. graveolens* had antispasmodic, antibacterial, antiulcer, diuretic, hypo-lipidemic and antioxidant activities [16].	The evaluation of the protective effect of the plant essential oils obtained from the seeds part against CCl_4 was carried out by using two groups of male albino rats. The first one was kept as a control (n = 6) and the second one had received for two weeks (twice a week) 2 mL/Kg of CCl_4 inducing chronic liver damage. Then, the last group were divided into subgroups (n = 6 each): Positive control and the treated group which had received orally 1 mL/Kg of *A. graveolens* essential oils for four weeks. The results showed that the essential oil had a potent hepatoprotective activity against CCl_4. It is able to inhibe the hepato-toxicity produced by CCl_4. In fact, the experiment showed that the treatment with this oil decreased significantly AST and ALT levels. However, it increased the total protein and albumin levels. The main compounds of the essential oil of this plant are carvacrol, carvone, limonene, *p*-cymen, dihydrocarvone, α-phellandrene, and dill apiole [15].	Carvacrol, carvone, limonene, *p*-cymene, dihydrocarvone, α- phellandrene, and dill apiole (16).

DISCUSSION

Liver tissue can be attacked by different toxins and molecules taken in overdoses which lead to dysfunction of this organ that is considered necessary for human life. However, there is some of natural product such as essential oils that are able to manage this disorder.

Liver injury was distinguished by many tests as the identification of ALT, ALP, bilirubin and AST levels [5]. Each test has its own indication, for example, high level of AST suggests that

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Table 1. Continued 2

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Artemisia halodendron Turcz *Artemisia sphaero-cephala Krasch* *Artemisia ordosica Kraschen*	Compositae	*A. halodendron Turcz*, *A. sphaerocephala Krasch* and *A. ordosica Kraschen* are medicinal herbs, used clinically to treat several health problems as intestinal obstruction, rheum arthritis and parotitis. They are perennial sub-shrub plants, [17] characterized by anti-oxidant, anti-bacterial and cytotoxic activities [18, 19]	These three species oil had a hepatoprotective activity against CCl_4 induced liver toxicity in mice. *Artemisia sphaerocephala Krasch* had a potent protective effect compared with the two other plant oils followed by *Artemisia ordosica Kraschen* oil and then *Artemisia halodendron Turcz* oil. *GC*/MS examination of the three plants, indicate the presence of Bisabolol oxide B, (+)-Trans-Nerolidol and α-Bisabolol in all these plants. However, n-Hexadecanoic acid, biphenyl and 9,12-Octadecadienoic acid were present only in *Artemisia halodendron Turcz*, oil [17].	Bisabolol oxide B, (+) - trans-nerolidol and α-bisabolol in all these plants. However, n-Hexadecanoic acid, biphenyl and 9,12-octadecadienoic acid were present only in *Artemisia halodendron* Turcz oil (18).
Artemisia capillaris	Asteraceae	*A. capillaris* has been used clinically for a long time to treat liver diseases such as hepatitis. It has been used also for anti-inflammatory, diuretic, choleretic, anti-apoptotic and antidiabetic purposes [20].	The essential oil of *A. capillaris* was evaluated *in vivo* by their hepatoprotective activity against CCl_4 induced liver damage in mice, by using bio-chemical methods. For this, the animals were divided into five groups: The control group were gavaged with sesame oil. Positive control, mice were gavaged with 10 mg/kg of bifendate tablets, for the other groups they were treated with 50 mg/kg and 100 mg/kg of *A. capillaris* oils dissolved in sesame oils. The treatment was done for six days. In the sixth day, the tested groups were injected intra-peritoneally with 0.2% of CCl_4 in sesame oil (10 mL/kg). The results showed that the administration of the essential oil of *A. capillaris* at a dose of 50 mg/kg and 100 mg/kg had a potent hepatoprotective effect against CCl_4 *in vivo*. Indeed, GC-MS analysis indicated that the oil contains 16.2% of citronellol, 13.9% of 1,8-cineole, 12.59% of camphor, 11.33% of linalol, 7.21% of α pinene, 3.99% of β pinene, 3.22% of thymol and 2.02%of myrcene [21].	Citronellol, 1,8- cineole, camphor, linalol, α-pinene, β-pinene, thymol and myrcene (23).

there is a loss of functional integrity in the liver, similar to the actions observed in muscle injury, cardiac infraction and viral hepatitis. ALT is a liver enzyme, that catalyzes the conversion of alanine to pyruvate and glutamate, it can detect liver damage [6].

In fact, there are four kinds of liver injury:

- Hepatocellular type, marked by an elevation of serum transaminase [5].
- Cholestatic and infiltrative types, characterized by an elevation in ALP with normal or mild decreasing in serum transaminases. Also, the cholestatic diseases were marked by an increasing of bilirubin levels [5].

The autoimmune liver injury is considered as a problem in the immune system when it attacks liver cells. The etiology of this disease remnant obscure. However, the most categories of

Table 1. Continued 3

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Athamanta turbith	Umbelliferae	*A. turbith* is present in southeastern Europe; it is characterized by three sub-species: *A. turbith* ssp. *turbith*, *A. turbith* ssp. *hungarica* (A_{thu}) and *A. turbith* ssp. *Haynaldii* (A_{tha}). In fact, A_{thu} and A_{tha} have been taking an importance in pharmacological studies particularly that was done by Tomié Ana and al in 2010 that have been focused on evaluation of the protective effect of the essential oils of those plants against CCl_4 inducing liver damage in Swiss Albino mice.	The oils were prepared by hydrodistillation from the dried powder of the mature fruit of the plants, and they were used as waster emulsions by Tween-80. Besides, CCl_4 was blended with olive oil. Actually, in this experiment ten groups are implemented: Three groups (H1, H2 and H3) were administrated respectively by 70, 140 and 280 μL/kg of A_{thu} oil. Then, L1, L2 and L3 groups have received A_{tha} oil at the same doses of the first essential oil. One group was administrated only by CCl_4 and two groups received only 140 μL/kg of one of the two essential oils. The last group represents the control (group not treated at all). Peroxidase (Px), CAT, glutathione peroxidase, xanthine oxidase (XOD) parameters were estimated in liver homogenate spectrophotometrically. While, AST, ALT, were measured in serum by commercial kits. The results of this experiment indicated that the administration of 140 μg/kg of the both oils, increased CAT activity. Indeed, the all tested doses showed a decreasing in Px activity. Furthermore, 70 μL/kg of A_{thu} and 140 μL/kg of A_{tha} reduced AST activity in comparison with the control [22].	Germacrene D terpinolene, myristicin, α-pinene, camphene, β-pinene, myrcene, terpinolene and *p*-cymene (25).
Boenning-hausenia albiflora	Rutaceae	*B. albiflora* is a species commonly found in the Himalayas and Pakistan. It was used traditionally as antiseptic and it being implicated on wounds and cuts.	The essential oil obtained by hydro-distillation of the aerial part of the plant was estimated by their protective effects against CCl_4 in Wistar albino rats *in vivo*, using different bio-markers: Alanine-aminotransferase (ALT), Aspartate-aminotransferase (AST), Alkaline phosphatise (ALP), LDH and bilirubin. The results indicated that the *B. albiflora* oil had a hepatoprotective activity. It has shown a resistance against free radicals induced by CCl_4 and then it protects the liver against oxidative damage [23].	-

this kind are autoimmune hepatitis, primary biliary cirrhosis and primary sclerosing cholangitis [69].

Hepatotoxines are able to produce oxidative stress by the formation of the LPO, inducing the depletion of ATP and the transition of mitochondrial membrane permeability which lead to the cell apoptosis, rupture and permeabilization of the membrane [70, 71]. Actually, the take at overdoses of the hepatotoxines increase the level of reactive oxygen species and induce the inhibition of antioxidant enzymes like SOD, GPx, GST, GSH and CAT; contribute to the initiation and the progression of liver injury [5].

This review includes the essential oils obtained from 27

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Table 1. Continued 4

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Carum carvi L	Apiaceae	*C. carvi L* is a medicinal herb commonly used as spices, food industries, pharmacy and in traditional medicine to treat flatulence, loss of appetite and gastrointestinal disorders. It has antispasmodic and antimicrobial effects [24].	*C. carvi* fruits used to prepare essential oils by hydro-distillation using n-hexane. To investigate the hepatoprotective activity of this oil against CCl_4 in mice *in vivo* three groups (n = 6) were treated orally with an appropriate solution. Each group was divided into two subgroups: Control group: Received saline solution. Group 2a received CCl_4 the group 2b received CCl_4 + *C. carvi* oil. Group 3a received only the oil of *C. carvi* (The other subgroups were used to evaluate the effect of *Coriandrum sativum*). Then, LPx, GSH, GSH/Px, Px, CAT, XOD, AST and ALT parameters were estimated in serum. The experiment results indicate that the treatment with *C. carvi* oil didn't induce in liver the pro-oxidative effect. Indeed, it's able to decrease XOD, GSH and CAT and increase GSH/Px, Px, and AST. The results concerning the oil analysis showed that the main compounds of *C. carvi* oil were carvone (78.8%), limonene (10.1%), cis-limonene oxide (1.8%), trans-carveol (1.3%) and menthone (1.2%) [25].	Carvone, limonene, cis-limonene oxide, trans-carveol and menthone (28).
Cinnamomum osmoph-loeum	Lauraceae	Taiwan is the origin of *C. osmophloeum* tree. It's characterized by an altitude between 400 and 1500 m [26]. It is used traditionally as a medicinal plant to treat inflammation, diabetes, and enteric infection [26]. Moreover, trans-cinnamaldehyde, (-)-aromadendrene, T-cadinol, and R-cadinol are the major bioactive compounds of *C. osmophloeum* essential oils.	Research was done on these constituents to evaluate their hepatoprotective effect against lipopolysaccharide/ D-Galactosamine induced acute liver injury in Mice *in vivo* compared with silymarin (Hepatoprotective agent). In this experiment, the animals were treated with 500 ng of LPS and 25 mg of D-Galactosamine and 250 μL of saline before the administration intraperitoneally of 100 μmol/kg of trans-cinnamaldehyde, 100 μmol/kg of (-)-aromadendrene, 100 μmol/kg of T-cadinol and 100 μmol/kg of R-cadinol. Then, AST, ALT, TNFα and IL-6 levels were measured from the serum. The results revealed that the treatment with 100 μmol/kg of the bioactive compounds of the oil decreased significantly in serum: AST, ALT, (TNFα), and IL-6 levels and they reduced the incidence of liver damage induced by lipopolysaccharide/ D-Galactosamine [27].	Trans-cinnamaldehyde, (-)-aromadendrene, T-cadinol, and R-cadinol (30).

Table 1. Continued 5

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Coriandrum sativum L	Apiaceae	*C. sativum L* is a medicinal herb commonly used as spices, food industries, pharmacy and traditional medicine to treat flatulence, loss of appetite and gastrointestinal disorders. It has antispasmodic and antimicrobial effects.	*C. sativum* fruits used to prepare essential oils by hydro-distillation using n-hexane. To investigate the hepatoprotective activity *in vivo* of this oil against CCl_4 in mice three groups (n = 6) were treated orally with an appropriate solution. Each group was divided into two subgroups: Control group: Received saline solution. Group 2a received CCl_4. Group 3b received CCl_4 + *C. sativum* oil. Group 3a received only the oil of *C. sativum* (The other subgroups were used to evaluate the effect of *C. carvi*). Then, LPx, GSH, GSH/Px, Px, CAT, XOD, AST and ALT parameters were estimated in serum. The results of the experiment indicate that the treatment with *C. sativum* oil increased LPx and Px, GSH, ALT and AST levels. Oil analysis results showed that *C. sativum* oil contains 74.6% of linalol, 5.9% of camphor, 4.6% of geranyl acetate, 4% of p-cymene, 2.8% of trans-geraniol, 1.2% of γ-terpinene and borneol [25].	Linalol, camphor, geranyl acetate, p-cymene, 2 trans-geraniol, γ-terpinene and borneol (28).
Croton zehntneri	Euphorbiaceae	*C. zehntneri* is an aromatic herb, natives in Northeastern Brazil. Used traditionally as appetizing, sedative and to treat gastrointestinal disorders.	Essential oil of this plant extracted from the leaves part, showed a significant hepatoprotective activity. So, to estimate this effect a research based on the use of rat model induced liver toxicity by acetaminophen was carried out. Indeed, rats were pretreated with different doses of the oil: 30, 100 and 300 mg/kg, and 750 mg/kg N, acetylcisteine for three times: 2, 24 and 48 hours followed by the injection of 500 mg/kg acetaminophen. GOT and GPT levels were measured from serum to evaluate this protective activity. GC/MS analysis of the oil indicates the presence of anethole (57.91%), estragole (27.94%), bicyclogermacrene (5.16%), β-caryophyllene (1.73%), myrcene (1.19%), germacrene D (1,17%), 1,8- cineole (0.77%), spathulene (0.62%), β-elemene (0.36%), globulol (0.30%), (E)-β-ocimene (0.27%), alloaromadendrene (0.24%) and α-phellandrene (0.23%). Furthermore, *C. zehntneri* oils were able to protect liver damage induced by acetaminophen. It can reduce GPT and GOT as compared with acetaminophen group [28].	Anethole, estragole, bicyclogermacrene, β-caryophyllene, myrcene, germacrene D, 1,8- cineole, spathulene, β-elemene, globulol, (E)-β-ocimene, alloaromadendrene and α-phellandrene (31).

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Table 1. Continued 6

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Cymbopogon citratus	Poaceae/ Gramineae	*C. citratus* is an aromatic plant, present in tropical and subtropical countries. Its essential oil was obtained from the leaves part [29]. *C. citratus* oil has anti-oxidant, anti-inflammatory, anti-malarial, analgesic and anti-convulsive effects [30, 31].	The hepatoprotective effect of this oil was examined by using acetaminophen induced liver damage in mice. Animals were pre-treated with three doses: 125, 250 and 500 mg/kg of the oil respectively and 200 mg/kg of silymarin (Standard drug) for seven days, followed by the injection of 250 mg/kg of the acetaminophen. ALT, AST, ALP and γ-glutamyl transferase markers were estimated from the serum to investigate the hepatoprotective effect of the oil. GC/MS and NMR spectroscopy was used to analyze the essential oil of *C. citratus*. The results obtained showed that the oil decreased AST, ALT and ALP levels as compared with the acetaminophen group which mean that *C. citratus* oil had a hepatoprotective activity against acetaminophen. Concerning the bioactive compounds present in the oil there are 24.98% of neral as cis-citral and citral B, 27.3% of geranial as trans-citral and citral A and 30.75% myrcene [29].	Neral as cis-citral and citral B. Geranial as trans-citral and citral A and myrcene (32).
Foeniculum vulgare	Umbelliferae	*F. vulgare* is an annual aromatic plant. The leaves, seeds and stems parts of this herb are comestible. In fact, dried fruits of the plant are commonly used in medicinal preparations to treat flatulence, bloating, spasmodic, gastrointestinal, pediatric colic and respiratory problems. It increases libido and relieved the menopause symptoms [32]. Moreover, it is used in cosmetic.	Several works have been done on *F. vulgare* oil in order to evaluate their protective activity against CCl_4 induced acute liver toxicity in rats showed that the plant oils have hepatoprotective action particularly that was done by Hanefi Özbek and al in 2003 and in 2004 [33, 34]. In fact, the experiment was focused on the use of three groups (n = 8) of rats: Control group: Animals were injected intraperitoneally with 0.2 mL of isotonic saline solution. Group 2: Rats have received 1,5 mL/kg of CCl_4 diluted in olive oil. Group 3: Rats have received 1.5 mL/kg + 0.3 mL/kg of the *F. vulgare* oil, which was prepared from the seeds powder by steam distillation. AST, ALT, ALP and bilirubin marker enzymes were measured from the serum during seven weeks for three times a week. The results indicated that *F. vulgare* essential oil has a potent protective activity against CCl_4. GC analysis of this oil showed the presence of 74.8% of (E)-anethole, 11.1% of limonene, 4.7% of methyl chavicol, 2.5% of fenchone, 1.3% of α pinene and 1.2% of (Z) -β-ocimene [33].	(E)- anethole, limonene, methyl chavicol, fenchone, α pinene and 1 (Z) -β-ocimene (36).

Table 1. Continued 7

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Hypericum scabrum	Hypericaceae	*H. scabrum* is a medicinal plant, which has a several therapeutic actions as anti-depressant, bronchodilator, management of cardiovascular disorder, antispasmodic, wound healing and antibacterial activities [35-37].	The essential oils of *H. scabrum* have been estimated for their hepatoprotectice effect on acetaminophen induced liver stress in rats. Animals were pre-treated with two doses: 100 and 200 mg/kg of the oil respectively, diluted in 400 mL of DMSO (Diméthylsulfoxyde), and 10 mg/kg of butylated hydroxytoluene (Positive control), followed immediately by the injection of 500 mg/kg of the acetaminophen dissolved in 400 mL of DMSO. SOD, CAT, GSH, LPO, FRAP markers have been estimated from the serum after 2, 4, 16 and 24 hours of the treatments. The results showed that LPO, FRAP and SOD levels were lowered in the group treated with the oil as compared with acetaminophen group. Then, the liver biopsies have confirmed the protective effect of the oils [38].	α- thujan, α- pinene, α- Fenchene, camphene, β-pinene, β- myrcene, α- phellandrene, α-terpinene, *p*- cymene, limonene, (Z) β- ocimene, (E) β- ocimene, γ- terpinene, terpinolene, borneol, terpin 4 ol, pulegone, thymol, carvacrol, α-cubebene, α- copaene, β-elemene, β- caryophyllene, α-humulene, germacrene-D, bicyclogermacrene, Δ cadinene, 1,4-cadinadiene, caryophyllene oxide and epi-α- cadinol (42).
Hyptis crenata	Lamiaceae	*H. crenata* leaves used traditionally to cure gastrointestinal and liver disorders [39]. Essential oil of this plant, obtained from aerial parts, contains 32.78% of camphor, 18.02% of 1.8-cineole, 13.37% of α-pinene and 12.86% of β-caryophyllene [40].	To estimate the hepatoprotective effect of this oil a research focused on the use of rat model produced liver dysfunctions by cecal ligation and puncture (CLP). Animals were divided into four groups treated with an appropriate solution every 12 hours for 24 hours: Sham, sham + 300 mg/kg of *H. crenata* oils, CLP + 300 mg/kg of *H. crenata* oils and CLP groups. ALT, ALP, CAT, SOD, glutathione peroxidase (GPx), LPO and malondialdehyde parameters were measured in hepatic tissue to investigate the oxidative stress in the liver. Then, the histological examination was carried out to confirm the results. The treatment with *H. crenata* oils have normalized the level of ALT, ALP and bilirubin and it inhibited the increasing of GPx and LPO, which mean that the plant oils had a hepatoprotective action on sepsis, induced liver injury [41].	Camphor, 1.8-cineole, α-pinene and β-caryophyllene (45).

plants belonging to 12 families as the table show: Lamiaceae (7 species), Asteraceae (6 species), Umbellifereae (3 species), Apiaceae (3 species), Rutaceae, Anacardiaceae, Bignoniaceae, Euphorbiaceae, Hypericaceae, Lauraceae, Poaceae and Zingiberaceae. These essential oils were shown that have an antioxidant activity which mean that contain the bioactive compounds able to neutralize free radicals and then decrease the oxidative stress in the liver.

According to this work, the major compounds isolated from some of these essential oils were cited. The most of those compounds belong to terpene class as Cineol, Carvacrol and thymol.

Cineol or Eucalyptol is also known as cajeputol, is a terpene oxide that found in some plant essential oil [73] particularly

Table 1. Continued 8

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Marrubium vulgare L	Lamiaceae	*M. vulgare* natives in Europe, Asia and in the Mediterranean area. It is used traditionally as expectorant, antispasmodic and in general respiratory infections. Furthermore, this plant is used also externally, in ulcers and wounds [24].	The essential oils of *M. vulgare L* obtained by hydro-distillation of the aerial parts of the herb, were tested for the hepatoprotective effects at a dose of 50 mg/kg body weight. For that, the oil was administered every day for 15 days before the injection of 5 mL/kg of CCl_4 "intraperitoneally". The chemical composition of *M. vulgare* oils was defined by "GC-MS" analysis. The results showed that the *M. vulgare* oil had a potent hepatoprotective effect which may be explicated by their powerful antioxidant activity. Indeed, this oil contains 36 components: 99.79% of the total oil profile, 20.11% of thymol and 15.66% of E,β-Farnesene which represent the main constituents [14].	β- Pinene, methyl chavicol, E- anethol, thymol, Carvacrol (15).
Oroxylum indicum L.	Bignoniaceae	*O. indicum L.* is a tree that growth in India, China, Malaysia, Thailand, Cochin, Ceylon, Indonesia, and Philippines [42]. In herbal medicine, *O. indicum L.* used to treat bronchitis, inflammation, respiratory diseases such as asthma, leucoderma, intestinal worms, fever, diarrhea and anal disorders [43]. Phytochemically, *O. indicum L* contains flavonoids as apigenin, baicalein, chrysin, oroxylin A, scutellarin and tetuin and it contains also cyclo-hexyl-ethanoids, pterocarpanoids, sterols and volatile oil [44].	The essential oil of this plant leaves showed a hepatoprotective effect against CCl_4 produced liver toxicity in rats. So, to evaluate this activity, serum ALT, ALP and AST were estimated of the tested animals. Actually, once dose of the oil was tested daily for seven days (10 mg/mL). The positive control was pre-treated with 25 mg/mL of the standard drug: Silymarin, followed by the injection of CCl_4. GC/MS examination of the essential oils showed the presence of 63.81% of oxygenated constituents as sesquiterpene ketones, esters, diterpene ketones, ketones, sesquiterpene alcohol, alcohols and sesquiterpene esters and 26.04% of non-oxygenated compounds like sesquiterpenes and aliphatic hydrocarbon [42].	Flavonoids as apigenin, baicalein, chrysin, oroxylin A, scutellarin and tetuin. Cyclo-hexyl-ethanoids, pterocarpanoids, sterols and volatile oil (49).

Achillea biebersteinii Afan, *Artemisia capillaris*, *Croton zehntneri*, *Hyptis crenata and Rosmarinus officinalis* essential oils. It is frequently used as an aromatic agent for food products and it is used by the pharmaceutical industry in the production of the drugs. Cineol has been used as a growth inhibitor and to treat the symptoms of respiratory tract diseases [72]. Indeed, there are several studies have shown that this compound has an anti-inflammatory and analgesic effects [73]. In addition, it has shown an inhibitory activity *in vivo* and *in vitro* on the production of inflammatory mediators such as cytokines, leukotrienes and prostaglandins from human blood monocytes stimulated by lipopolysaccharides [74].

Carvacrol or 2-methyl-5-(1-methylethyl)-phenol is monoterpenic phenol occurs in some essential oil plants belonging particularly of the family Lamiaceae (*Ajuga iva*, *Thymus vulgaris*), Asteraceae (*Achillea biebersteinii Afan*) and Apiaceae (*Anethum graveolens*). It is used in sweets, beverages, and chewing gum as a flavoring agent [75]. This bioactive compound has several pharmacological activities including antioxidant [76], anti-inflammatory [77], antimicrobial [78], antibacterial, anti-

Table 1. Continued 9

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Pimpinella anisum	Umbelliferae	*P. anisum* is a medicinal plant, distributed in Iran, Egypt, Greece and Turkey [44]. It is used traditionally as anti-inflammatory, analgesic and anticonvulsant agents [45, 46]. In some works, the pharmacological properties of *P. anisum* oils obtained from its seeds have been evaluated. It has been found that it has several biological activities as antioxidant effect [47].	It was reported that diethyl ether extract of *P. anisum* seeds improved CCl_4 induced liver damage. Moreover, the essential oil of this plant can protect rats from aspartame produced liver injury. So, to be sure of this hypothesis, Akram Jamshidzadeh and al in 2015 have investigated the effect of this oil against CCl_4. Rats were pre-treated with two different doses of the *P. anisum* oil: 20 mg/kg and 100 mg/kg, respectively, and 1.5 mL/kg of CCl_4 dissolved in olive oil. Concerning, the control group was pretreated with 1.5 mg/mL of the olive oil. Then, the serum biomarkers were estimated after 24 hours of CCl_4 injection and the histological examination was performed in order to confirm the obtained results. The experiment results revealed that CCl_4 increased serum transaminases, LDH and LPx. Thus, the treatement with the oil at dose of 20 mg/kg of *P. anisum* oil had no significant action on GSH and LPx depletion. Nevertheless, the medication with 100 mg/kg of the essential oil was able to improve the different parameters that have measured [48].	Linalool, estragole, cis-anethole, trans-anethole, γ-himachalene, zingiberene, anisylacetone, o-isoeugenol and butanoic acid and 2-methyl-, 4-methoxy-2-(3-methyloxiranyl) phenyl ester (54).
Pistacia chinensis ssp.	Anacardiaceae	*P. chinensis ssp* is a tree that found in the Himalayas at an altitude of 352-400 m. Galls occurred in the leaves of this plant, have aromatic and medicinal properties; they are used to treat several health problems as diarrhea, asthma, cough, fever, nose bleeding, vomiting, loss of appetite, scorpion stings. Also, it is used with honey to cure liver diseases [49]. It was noted that they had an antioxidant, antibacterial, anti-inflammatory, analgesic and immune modulator effects [49-51].	There is a study that had focused on investigation *in vivo* of the hepatoprotective effect of *P. chinensis ssp* essential oils; obtained from leaf galls, against CCl_4. Mice were pre-treated respectively, with three doses: 0.05, 0.1 and 0.2 mL/kg of the oil, and 25 mg/kg of silymarin for seven days, then they were injected with 1.5 mL/kg of CCl_4 after 2 hours of the treatments. The results showed that the treatment with CCl_4 increased bilirubin, ALT, ALP and AST levels as compared with the control group which was treated with sesame oils, whereas, the pre-treatment with *P. chinensis ssp* oils reduced significantly this elevation. The histological examination of the liver mice indicated that the treatment with the oil at 0.1 and 0.2 mL/kg was effective as Silymarin. GC/MS analysis indicated that α-pinene, β-pinene, γ-terpinene, terpinene-4-ol, α-terpineol, Δ^3-carene and limonene are the major constituents of *P. chinensis ssp* oils [49].	α-Pinene, camphene, β- pinene, sabinene, Δ^3- carene, β- myrcene, α- terpinene, limonene, β-phellandrene, γ-terpinene, *p*- cymene, α-terpinolene, α-longipinene, endobornyl acetate, trans-caryophyllene, terpinene-4-ol, trans- pinocarveo, iso- borneol, verbenone, borneol, α-terpineol, bicyclogermacrene, myrtenol and spathulenol (55).

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Table 1. Continued 10

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Rosmarinus officinalis	Lamiaceae	*R. officinalis* is a perennial shrub, evergreen. It possesses a lot of therapeutic applications in traditional medicine, it has been reported that it is able to treat diabetes, respiratory diseases, stomach problems and inflammatory disorders. Actually, Rosemary species has been extensively accepted as one of the most species that had an anti-oxidant activity [52].	The water and ethanolic extracts of the plant have a hepatoprotective activity. So, other research interests of the essential oils of this plant were performed to evaluate the hepatoprotective activity of the aerial parts of *R. officinalis* at a dose of 50 mg/kg body weight. The oil was got by hydro-distillation. Moreover, it was administered to animals every day for 15 days before the injection of CCl_4 "intraperitoneally". The chemical composition of *R. officinalis* oils was defined by GC-MS examination. Therefore, the results showed that *R. officinalis* oil contains 19 components: 99.63% of the total oil profile, 35.21% of 1,8-cineol and 24.71% verbenone which are the main constituents of this oil. Furthermore, the experiment indicated that *R. officinalis* oils possess a significant hepatoprotective activity [14, 52].	α-Pinene, camphene, 1,8-cineole, terpinolene, linalool, camphor, isoborneol, borneol, lavandulol, verbenone, citronellol, *p*-mentha-1-en-9-ol and geranyl formate (15).
Satureja rechingeri	Lamiaceae	*S. rechingeri* is a medicinal herb that distributes in Europe, northern Africa, and Asia Minor [53]. It is used traditionally in Iran for curing many diseases such as nausea, infectious disorders, muscle pains and cramps [54]. Many researches showed that the active compounds of this plant have beneficial properties like an anti-inflammatory, antioxidant, anti-noceceptive, antiviral, antifungal, antibacterial, antidiarrheal, antispasmodic and vasodilatory effect [53, 55].	*S. Rechingeri* essential oils had a hepatoprotective activity against acetaminophen induced hepatotoxicity in rats. In this study, the animals were pre-treated with one dose of the essential oil: 20 mg/kg diluted in 400 mL DMSO. Followed by the administration of 500 mg/kg acetaminophen dissolved in 400 mL DMSO after 14 days of the treatment. The results indicated that acetaminophen decrease the activities of GPx, glutathione reductase (GR), SOD and GSH content and increased AST activity and the level of FRAP and LPO. While, the treatment with the essential oil protected effectively the liver against toxicity induced by the hepatotoxine. It is increased GSH, SOD, GPx and GR levels. Then, the histopathological examination was confirmed this activity, it showed a decreasing in the number of necrotic cells and of degenerated lobules [53].	α-Thujene, α-pinene, camphene, β-pinene, β-myrcene, α-terpinene, *p*-cymen, limonene, γ-terpinene, linalool, borneol, terpinen-4-ol, β-fenchyl acetate (endo), neral, geraniol, thymol, Carvacrol, thymol acetate, E-caryophyllene, caryophyllene oxide (62).

viral [79], antitumor [80] and hepatoprotective [75] properties.

Thymol or paramethyl-isopropyl-phenol is the main bioactive compounds of the plant essential oils as *Artemisia capillaris*, *Marrubium vulgare L and Thymus capitatus* essential oils. Thymol was shown that had a hepatoprotective activity against CCl_4 induced liver toxicity in mice. In fact, the administration of thymol at a dose 300 mg/kg in mice, shown an inhibition of LPO that induced by CCl_4 [81].

Table 1. Continued 11

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Thymus capitatus	Labiatae	*T. capitatus* is an herbaceous shrub, perennial used traditionally to treat several health problems. It is known as antitussive, antipyretic, carminative and disphoretic [56]. It was exploited for their reputation as medicinal plants and for their oils [57].	The aerial parts of this plant were subjected to hydrodistillation for obtaining the essential oils to evaluate it by their hepatoprotective activity. Fifty mg/kg body weight is the dose of the oil that was tested to examine this activity. For this reason, the oil was administered every day for 15 days before the injection of 5 mL/kg of CCl_4 "intraperitoneally". The chemical composition of *T. capitatus* oils was determined by "GC-MS". The results indicated that the essential oils possess 27 constituents among these components: 99.48% of the total oil profile and 90.15% of thymol. Moreover, the experiment showed that the essential oil of *T. capitatus* had a significant hepatoprotective activity [14].	α and β- pinene, β-myrcene, α-phellandrene, α-terpinene, *p*-cymene, 1,8-cineole, terpineolene, dehydro-sabina ketone, iso-3-thujanol, neo-3- thujanol, camphene hydrate, isoborneol, neo-3- menthol, neo-iso- isopulegol, neo-Dihydro carveol, verbanol, E- dihydro carvone, Z-ocimenone, thymol and carvacrol (15).
Thymus vulgaris	Lamiaceae	The leaves of *T. vulgaris* have an important value in nutrition; particularly it is used as a spice, freshly or dried. It was used also in traditional medicine as antiseptic, antimicrobial, anti-inflamatory, carminative and antioxidative activities [58, 59].	The fresh leaves of *T. vulgaris* were used to prepare the essential oil. To assess the hepatoprotective effect of this oil, six groups of mice (n = 5) were used. Each group was treated for seven days: Group 1 represents the control. Group 2: the mice were administrated by *T. vulgaris* oil vehicle saline (contains 0.1% of Tween 80). Groups 3, 4 and 5: were treated with the oil at different doses: 125, 250 and 500 mg/kg respectively. The last group received 200 mg/kg of silymarin (Standard drug). All animals were fasted for 8 hours after the treatment time and then they were administrated orally by 250 mg/kg of the acetaminophen induced liver damage, exception the control group which was received saline contained 0,1% of Tween 80. After 12 hours, the levels of AST, ALT and ALP bio-markers were measured. GC/MS analysis was carried out to identify the compounds present in the oil. The results showed that the treatments with 250 and 500 mg/kg of *T. vulgaris* oil for seven days reduce ALT, AST and ALP levels as compared with the control. Moreover, the essential oil indicated the presence of 45.54% of carvacrol, 22.96% of α terpineol and 14.29% of endo-borneol [6].	α-Pinene, camphene, β-myrcene, carene, *p*-cymene, γ-terpinene, α-terpineol, thymol, caryo-phyllene, Humulene (67) carvacrol, α terpineol and endo-borneol (6).

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Table 1. Continued 12

Scientific names	Family names	Plant information	Experimental assay	Active compounds
Zingiber officinale	Zingiberaceae	*Z. officinale* is a medicinal herb known by its rhizome which used as spice. It has several physiological properties like decreasing nausea [60], preventing cardiovascular disorders [61], inhibiting the proliferation of cancer cells [62]. Also, it improves the intestines, stomach, liver functions [63, 64] and it is used to treat diabetes [65] and atherosclerosis [61]. *Z. Officinale* essential oils are commonly used in cosmetics and in food. Furthermore, it has been declared that ginger oil had an antioxidant and anticancer effect [66, 67].	The hepatoprotective effect of this oil was evaluated; using Lieber-DeCarli diet induced alcoholic fatty liver disease and high fat diet induced nonalcoholic fatty liver disorder. The animals were divided into three groups: Control group in which the mice were fed with normal liquid diet. Group 2 contains animals that they fed with ethanol containing Lieber-DeCarli diet. Then, they are treated with 2.5 or 12.5 mg/kg of ginger oil or with 0.375 or 1.875 mg/kg of citral mixed with olive oil, for four weeks. The normal group was received only olive oil. Liver biochemical parameters and liver enzymes have been measured. Then, the histological examination was performed from liver biopsy to confirm the results obtained [63]. Regarding the effect of ginger oil against nonalcoholic fatty liver disease, the animals were divided into groups (n = 8) and they received 12.5, 62.5 and 125 mg/kg of ginger oil respectively, and 2.5 or 25 mg/kg of citral after two weeks of feeding. The medication was done for 12 weeks. Then, they received olive oil with the same volume. The results showed that *Z. Officinale* essential oils and citral had a hepatoprotective effect against alcoholic fatty liver disease. Besides, the administration of ginger oil at a dose 62.5 and 125 mg/kg and the treatment with 25 mg/kg of citral reduced significantly hepatic liver accumulation [68].	*Z. Officinale* essential oil contains β-zingiberene, 1,8-cineole+limonene+β-phellandrene, geraniol, neral, β-bisabolene and β-sesquiphellandrene (77).

CONCLUSION

In conclusion, this study classifies 27 plants belonging to 12 families: Lamiaceae (7 species), Asteraceae (6 species), Umbellifereae (3 species), Apiaceae (3 species), Rutaceae, Anacardiaceae, Bignoniaceae, Euphorbiaceae, Hypericaceae, Lauraceae, Poaceae and Zingiberaceae. Those plants allow giving the essential oils which have been studied by their hepatoprotective activity.

The review covers also the major compounds isolated from some of these essential oils. The most of those compounds belong to terpene class; among these active constituents: Cineol, Carvacrol and thymol. Thus, the different essential oils that have been cited in this review were shown that have an antioxidant activity which play a key role in the reducing of the oxidative stress induced by the hepatotoxines. However, several efforts must be made to value these essential oils and identify the active constituents responsible for the hepatoprotective activity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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