Hepatoprotective Essential Oils: A Review

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Objectives: Several toxins and molecules are able to damage the liver, causing the hepatotoxicity. 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.
### Table 1. Hepatoprotective essential oils

| Scientific names | Family names | Plant information | Experimental assay | Active compounds |
|------------------|--------------|-------------------|-------------------|------------------|
| *Achillea biebersteinii*<br>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 (CCl4) 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 CCl4 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 α-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*<br>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). |
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
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
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
### 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 osmophloeum* | 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, TNF$_\alpha$ 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, (TNF$_\alpha$), 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. | 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 CCl4 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 CCl4. Group 3b received CCl4 + 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). |
Table 1. Continued 6

| Scientific names | Family names   | Plant information                                                                 | Experimental assay                                                                                                                                                                                                                                                                                                                                 | Active compounds                                                                                     |
|------------------|----------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| Cymbopogon       | Poaceae/        | C. citratus is an aromatic plant, present in tropical and subtropical countries. Its  | 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].  |
| citratus          | Gramineae       | 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]. |                                                                                                                                                                                                                                                                                                                                                         | Neral as cis-citral and citral B. Geranial as trans-citral and citral A and myrcene (32).            |
| Foeniculum        | 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 CCl4 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 CCl4 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 CCl4. 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). |
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 particularly

| 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 hepatoprotective 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, bicyclagermacrene, 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). |
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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 B

| 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 CCl4 “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, diarrhoea 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 CCI4 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 CCI4. 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). |

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Table 1. Continued

| 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 CCl₄ 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 CCl₄. 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 CCl₄ 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 CCl₄ injection and the histological examination was performed in order to confirm the obtained results. The experiment results revealed that CCl₄ increased serum transaminases, LDH and LPx. Thus, the treatment 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, anisyacetone, 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 CCl₄. 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 CCl₄ after 2 hours of the treatments. The results showed that the treatment with CCl₄ 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, Δ⁹-carene and limonene are the major constituents of *P. chinensis* ssp oils [49]. | α-Pinene, camphene, β- pinene, sabinene, Δ⁹-carene, β- myrcene, α- terpineole, 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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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 CCl₄ 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 CCl₄ [81].

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 CCl₄ “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-cineole 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), nerel, geraniol, thymol, Carvacrol, thymol acetate, E-caryophyllene, caryophyllene oxide (62). |
| 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 CCl₄ “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-oicimone, 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-inflammatory, 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, caryophyllene, Humulene (67) carvacrol, α-terpineol and endo-borneol (6). |
In conclusion, this study classifies 27 plants belonging to 12 families: Lamiaceae (7 species), Asteraceae (6 species), Umbelliferae (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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