Review Article

Role of Herbal Remedies in liver Fibrosis: What is the Evidence?

Barghi M[1], Alemzadeh E[2,3*]

1. Department of Biochemistry, Faculty of Veterinary Medicine, Shiraz University, Shiraz, Iran
2. Cellular and Molecular Research Center, Birjand University of Medical Sciences, Birjand, Iran
3. Department of Medical Biotechnology, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran

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Abstract

Liver fibrosis is a disease that is created due to the excessive accumulation of extracellular matrix proteins such as collagen. Advanced liver fibrosis leads to cirrhosis and eventually to liver cancer which are irreversible conditions. Hence, attention to initial stages of disease and its treatment has a vital role in these patients. Synthetic drugs utilized to remedy liver diseases often have side effects and thus, treatment method should be changed to alternative medicines, especially herbal remedies or their derivatives. Today alternative medicine has gained special attention, because of their lasting term curative power and poor side effects. In this review, we explained some plant-derived compounds which play an effective role in healing of liver injuries. We also somewhat mentioned the mechanism of action of these components. Future works should focus on the molecular pathways these compounds in order to determine the potential applications of these medicines.

Keywords: alternative medicine, herbal remedies, liver fibrosis

Introduction

Liver is an important organ in human body that regulates glycogen accumulation, plasma protein production and detoxification (1,2). Since liver is involved in the detoxification of chemicals, it is exposed to many diseases. The statistical study showed that more than 10% of the world population suffers from liver diseases. Hepatitis, fatty liver, fibrosis, cirrhosis and alcoholic are the most common liver diseases (1,3).

Since synthetic drugs utilized to remedy liver diseases often have side effects, herbal medicine has been considered as an alternative method in treating liver disease. The advantages of herbal medicine are their safety and lasting term curative power. It is shown that natural compounds almost are hepatoprotective agents and can be considered for treating liver disease. Herbal remedies have a fundamental function in the treatment of liver disease in Europe and US (1,3).

Among liver diseases, fibrosis is more important. It is the result of reversible repair response to a chronic liver injury that is diagnosed by extracellular matrix accumulation (4,5). The variety of causes of liver injury can be viral, chronic alcoholism, drug induced, cholestatic, toxins, infections, non- alcoholic steatohepatitis (NASH), auto-immune hepatitis (5,6). Hepatic stellate cells (HSCs) after liver injury converted to myofibroblast like phenotype with characteristics of proliferation, fibrogenesis and contractility that lead to fibrosis (5,7). Fibrosis can lead to cirrhosis and eventually to liver cancer. Rapid rise in deaths from liver disease 0.8 million deaths in 1990 and 1.2 million deaths in 2013, has reported (8). The fifth common cancer is Hepatocellular carcinoma (HCC). Therefore, attention to liver function is in priority (9). Today, alternative medicine has been

***Corresponding Author Alemzadeh Esmat,** Department of Medical Biotechnology, Faculty of Medicine, Birjand University of Medical Sciences, Birjand, Iran.
Email: esmat.alemzadeh@gmail.com
https://orcid.org/0000-0001-5287-4760

considered as an effective therapeutic strategy in medical remedy (10-12). Extensive use of alternative medicine in chronic diseases prevents illness associated with ordinary health care (13). Almost a large number of people use herbal medication for their early health care (1). The beneficial effects of a number of plant derivatives against hepatic fibrosis in cell culture (*in vitro*) and in animal models (*in vivo*) have been proven (1,14-16). The present review article evaluated the effects of forty plants or their ingredients on attenuation of liver fibrosis in *in vitro* and *in vivo* studies.

Materials & Methods

To conduct this review article, relative articles were gathered on liver fibrosis since 1988 to 2019 from PubMed database, Google Scholar search. Search by keywords such as plant, plant extracts, herbs, alternative medicine, liver fibrosis and anti-fibrotic activity occurred.

Results

The use of medicinal plant-based products and derivatives is considered as a convenient and effective method for improving liver fibrosis. Forty articles were included in this study. The articles were assessed and summarized in Table 1. However, we explained some of the most important medicinal plants such as silymarin, armepavine, plumbagin, total saponins, Puerarin rhein, glycyrrhetinic acid, ginseng, crocin and crocetin, resveratrol, curcumin, and salvianolic acid in the discussion.

Table 1. The names of the herbs/botanicals together with the extract used or the compound isolated from a particular herb.

No	Plant	Part/Extract/ Active ingredient	Experimental model	Type of study	Biomarkers/parameters affected	Ref.
1	Gundelia tournefortii	hydroalcoholic extract	CCl4 induced	In vivo	↓ serum AST, ALT, LDH and alleviation of histopathological damages of liver.	(17)
2	Silybummarianum	Silymarin	CCl4 induced	In vivo	↓ serum AST, ALT and the liver hydroxyproline and CTGF.	(18)
3	Salvia miltiorrhiza	water-soluble extract	CCl4 induced	In vivo	↓ the mRNA expression TGF-b1,TIMP 1,procollagen)of liver.	(19)
4	Rosa laevigata Michx Fruit	total saponins	CCl4 induced	In vivo	↓the liver hydroxyproline, α-SMA, collagen I, collagen III and FN.	(20)
5	Silybummarianum and Sitagliptin	Silymarin and Dipeptidyl peptidase 4 inhibitor (DPP4-I),	CCl4 induced	In vivo	↓serumALT, AST, ALP, and GGT, ↓liver TGF-b1, 4-hydroxyproline, MDAand↓ SMA expression.	(21)
6	Coriandrum sativum	leaf extract	CCl4 induced	In vivo	↓serumALT, AST and TBARS levels. ↑liver enzymesactivity SOD, CAT.	(22)
7	Pomegranate peels	Methanolic extract	CCl4 induced	In vivo	↓serumALT, AST and TB ↓ liver Hydroxyproline and .↓serum levels ofHA, LN and PC III as the indexes of liver fibrosis	(23)
8	Pueraria lobata	Puerarin	CCl4 induced	In vivo	↓serum ALT, AST, ALP,LDH and ↑liver enzymes activity SOD ,CAT ,GPX	(24)

9	Aloe vera and Silybum marianum Against	Aloe vera and silymarin.	CCl4 induced	In vivo	↓the mRNA expression of TLMP, TNF-alpha, iNOS. ↓serum ALT, AST and ↓liver hydroxyprolin.	(25)
10	Gan-fu-kang (GFK)	Angelica	CCl4 induced	In vivo	↓ serum ALT, AST, HA, LN, PCIII, ↓ the mRNA expression of α-SMA,TIMP liver	(26)
11	PienTze Huang Gan Bao (GB)	silymarin	CCl4 induced	In vivo	↓serum ALT, AST, ALP, GGT. ↓the mRNA expression of TNF-alpha, IL-1 beta.	(27)
12	Taraphochlamys affinisa	total saporins	CCl4 induced	In vivo	↓ serum ALT, AST,ALP , TNF-alpha and liver MDA	(28)
13	Wood fordia Fruticosa Kurz flowers	Methanolicextrac	CCl4 induced	In vivo	↓ serum ALT, AST ALP, LDH and ↓Liver Hydroxyproline and MDA	(29)
14	Prunella Vulgaris	Aqueous Extract	CCl4 induced	In vivo	↓ serum ALT, AST, IL-4,IL-8, MMP, PDGF, TGF-beta ,HA,TNF-alfa	(30)
15	Artemisia capillaris	Aqueous Extract	CCl4 induced	In vivo	↓ serum ALT, AST, ALP, ↓ liver Hydroxyproline and MDA. ↑ activity SOD ,CAT , liver, ↓ the mRNA expression TGF-beta , PDGF-beta	(31)
16	Rhus javanica	Ethanol extract	Activated HSCs	In vitro	↓the mRNA expression Col 1 a2, TGF-b, a-SMA	(32)
17	Punica granatum	Peel	Biliary obstructed	In vivo	↓serum AST, ALT, LDH and ↓ liver MDA, MPO activity and collagen	(33)
18	Plumbago zeylanica	Plumbagin	CCl4 induced	In vivo and in vitro	↓the mRNA expression phosphorylation EGFR , STAT3 and α-SMA, EGFR in both fibrotic liver and HB-EGF treated HSC-T6 cells.	(34)
19	Pureria lobata	Puerarin	Alchol þ CCl4 induced	In vivo	↓serum AST, ALT, mRNA expression bcl-2	(35)
20	Rheum officinale	Rhein	CCl4 induced	In vivo	↓serum ALT,, HA, III (PC-III), and ↓mRNA expression alpha-SMA, TGF-beta1 liver,	(36)
21	Turmeric	Curcumin	CCl4 induced	In vivo	↑total glutathione.↓serum AST, ALT.	(37)
22	Salvia miltiorrhiza	Salvionolic acid	CCl4 induced	In vivo	↓the mRNA expression TGF-b1, PCI and III and TIMP liver	(38)
23	Glycyrrhiza glabra	Glycyrrhetinic Acid	CCl4 induced	In vivo	↓serum ALT, AST, ↑mRNA expression Nrf2 its target genes such as SOD3, CAT	(39)

24	Panax ginseng	Ginseng	CCl4 induced	In vivo	↓serum ALT, AST, and m RNA expression TGF-b, a-SMA	(40)
25	Nelumbo nucifera	Armepavine	TNF-a or lipopolysaccharide and bile duct ligation	In vivo and in vitro	↓mRNAexpression, of TNF-α- , α-SMA and collagen 1α2, in HSCs. And TGF-β1, TIMP1, and collagen 1α2, liver	(41)
26	Haobieyanqy in Ruanjian Decoction	Whole plant extract	CCl4 induced	In vivo	↓Serum HA, CIV , PCIII , LN, and↓the mRNA expression, TGFβ1 and Smad3	(42)
27	Arachniod esexilis	ethanol extract	CCl4 induced	In vivo	↓Serum ALT, AST and MDA liver, ↑SOD activity liver	(43)
28	lumnitzera racemose	Leaf extract	CCl4 induced	In vivo	↓Serum ALT, AST, ALP, LDH	(44)
29	Mistletoe (Viscum coloratum	Mistletoe.extract	CCl4 induced	In vivo and in vitro	↓mRNA expression, TGFβ1, TGFβ1 receptor, α-SMA liver, TGFβ1,TGFβ1 receptor, α-SMA, smad 2, TIMP in vitro	(45)
30	Bupleurum falcatum	saikosaponin-d	CCl4 induced	In vivo	↓Serum ALT, HA,LA, TG, and liver hydroxyprolin↓ mRNA expression TNF- α ,IL-6 liver	(46)
31	Jin SanE	Radix curcumae,	CCl4 induced	In vivo	↓Serum ALT,AST,HA, ↓mRNA expression TGFβ1, smad 3 liver	(47)
32	Zataria multiflora Boiss	essential oil	CCl4 induced	In vivo	↓Serum ALT, AST, GGT, ALP, TG , HA, TGFβ1, and liver HA, TGFβ1, hydroxyprolin , MDA	(5)
33	Carthamus tinctorius	Carthamus red	CCl4 induced	In vivo	↓Serum ALT,AST,ALP, ↑mRNA expression Nrf2 and activity GSH liver, ↓ MDA.	(48)
34	Grape	Resveratrol	N'-nitrosodimethylamine (NDMA)	In vivo	↓Serum AST, ALP, ALT bilirubin, and liver protein carbonyl, hydroxyproline, ↑glycogen, SOD, and ATPases activity liver	(49)
35	Crocus sativus (saffron)	Crocin and crocetin (saffron extract)	CCl4 induced	In vivo	↑activities SOD, CAT, ↑ GSH and ↓MDA liver	(50)

36	Pueraria lobata (Willd.), Salvia miltiorrhiza, Schisandrachinensis, and Silybummarianum	A mixture of extracts from four kinds of Chinese herbs,	Alcoholic and CCl4induced	In vivo	↓mRNA expression, TGFβ1, Smad2, Smad3, Smad7, TIMMP 1, ↑mRNA expression MMP13, ↓Serum levels of, HA, LA,, and hydroxyproline	(51)
37	turmeric	Curcuma	CCl4 induced	In vivo	↓Serum AST, ALP, ALT, ↓mRNA expression, TLR2, TLR4, a-SMA Smad2, phosphorylated Smad2, Smad3, TGF-b, and CTGF liver	(52)
38	Yi Guan Jian	aqueous extract	CCl4 induced	In vivo	↓Serum AST, ALT, MDA, TNF-α, IL-6, IL-1β and ↑SOD activity and ↓expression of MAPK/NF-κB pathway	(53)
39	Rhusverniciflua ,Eucommiaulmoides	aqueous extract	CCl4 induced	In vivo	↓Serum AST, ALT, GGT, TG, cholesterol, LDL- and ↑activities SOD , CAT , ↑GSH liver	(54)
40	Hydrocotylesibthorpioides	genistein	CCl4 induced	In vivo	↓Serum AST, ALT, HA, TNF-α, IL-6, IL-1β and ↓mRNA expression TMPP, TGFβ1, α-SMA liver	(55)

List of abbreviations given in the Table: ↑= Increase; ↓= Decrease; AST = Aspartate transaminase; ALT = Alanine transaminase; LDH=Lactate dehydrogenase; CTGF = Connective tissue growth factor; TGF-b = Transforming growth factor beta; TIMP-1 = Tissue inhibitor of metalloproteinase 1; a-SMA = Alpha smooth muscle actin; FN = Fibronectin; ALP = Alkaline phosphatase; GGT= Gamma-glutamyl transferase; MDA =Malondialdehyde;SOD= superoxide dismutase; CAT= catalase;TB= total bilirubin; HA= Hyaluronic acid; LN= laminin; PCIII= precollagen III; GPx=Glutathione peroxidase;TNF-a=Tumor necrosis factor alpha; iNOS = Inducible nitric oxide synthase; IL-1 = Interleukin 1; IL-4 = Interleukin4; IL-8= Interleukin 8;
PDGF-b = Platelet derived growth factor beta; MPO= myeloperoxidase;EGFR= external growth factor receptor; HB-EGF= heparin-binding EGF-like growth factor; Nrf2 = Nuclear factor erythroid-2-related factor 2 ; TG= triglyceride ; CIV= type IV collagen ; MMP-13 =Matrix metalloproteinase 13;GSH= glutathione;

Discussion

Activation of hepatic stellate cells involves two main stages: i) onset and ii) perpetuation. The onset is rapid alterations in gene expression and phenotype. HSCs receive paracrine stimulation from of the cells in their neighborhood (56). Figure 1 shows the interaction a number of cells with hepatic stellate cells in order to activate HSCs to myofibroblast-like phenotype. Kupffer cells activate HSCs and cause synthesis of ECM proteins by these cells through the actions of cytokines, such as transforming growth factor (TGF-β) (17-19), tumor necrosis factor (TNF-α), and matrix metalloproteinase (MMP) (57). In addition, kupffer cells release reactive oxygen species (ROS), which can cause HSCs activation and collagen synthesis (56). TGF-β is the main fibrogenic cytokine released by kupffer cells, endothelial cells and hepatocytes (1,58). In addition, TGF-β/Smad signaling pathway is the main pathway of TGF-β1 (59-62). Smads as transcription factors are TGF-β receptor substrates with the ability to transmit signals.

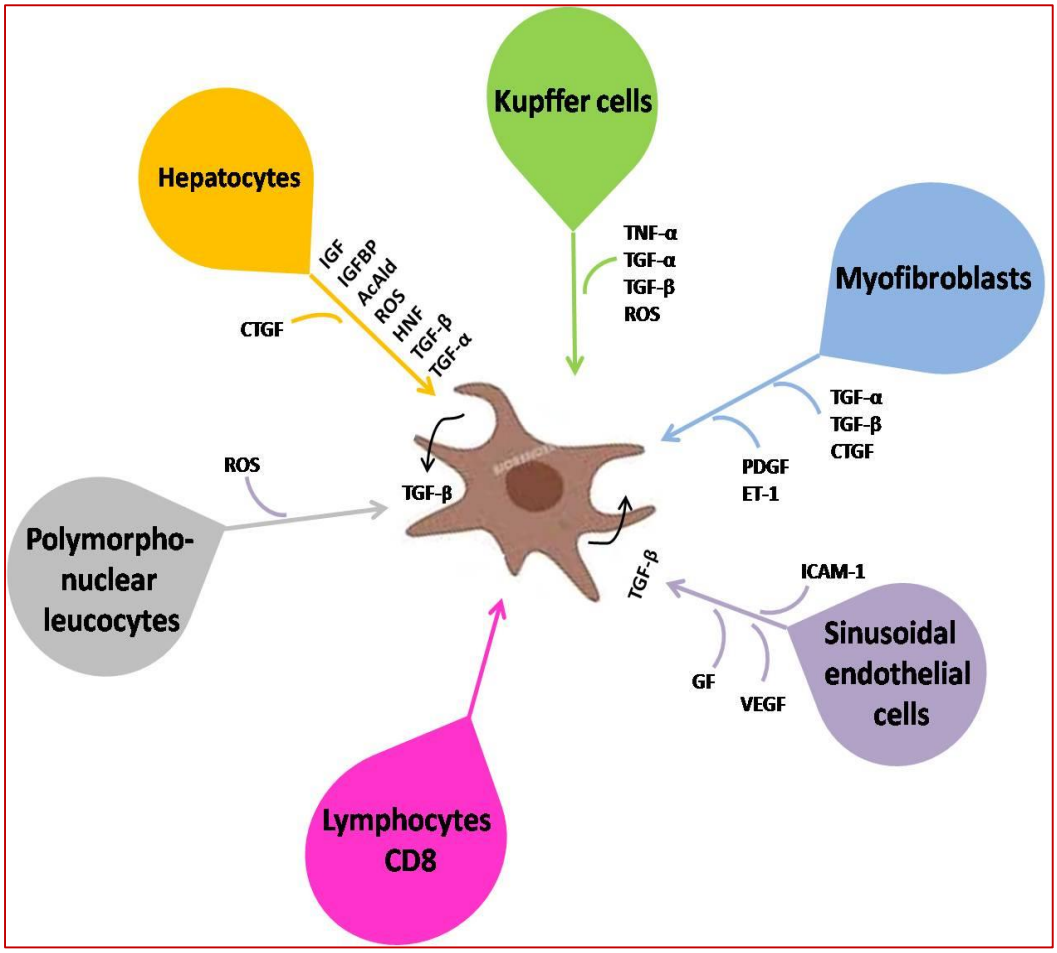

Figure 1. The most important paracrine mediators that activate hepatic stellate cells. *IGF*, insulin-like growth factor; *IGFBP*, insulin-like growth factor binding protein; *ROS*, reactive oxygen species; *HNE*, hydroxynonenal; *TGF*, transforming growth factor; *TNF*, tumor necrosis factor; *PDGF*, platelet-derived growth factor; *ET*, endothelin; *CTGF*, connective tissue growth factor; *GF*, growth factor; *ICAM*, intercellular adhesion molecule; *VEGF*, vascular endothelial growth factor.

Smads-complex accumulate in the nucleus and increase the expression of genes associated with ECM proteins (1,42,62,63). Myofibroblasts release platelet derived growth factor (PDGF) and endothelin-1. PDGF causes proliferation of HSCs and liver fibrosis. Liver fibrosis in experimental animals has been decreased by inhibition of PDGF (1,56,64). PDGF activates c-Jun N-terminal kinase (JNK) signaling and extracellular signal-regulated kinase (ERK) resulting in both JNK and ERK activations induce HSCs proliferation (56,65). Endothelial cells so can activate HSCs by inducing TGF-β active profibrogenic form (56). Endothelin-1, by its type A receptor stimulates fibrogenesis (1,66). Injured hepatocytes release ROS during liver fibrosis and result in collagen production in HSCs. Neutrophils also release ROS, which may stimulate collagen synthesis by HSCs (56,67). It is shown that the administration of antioxidants can reduce HSCs activation (56,68).

After liver injury, leukocytes accumulate to the injury area. Lymphocytes, especially CD4 T-helper (Th) produce cytokines, including interferon (IFN)-γ, TNF, and interleukin (IL)-2, IL-4, IL-5, IL-6, and IL-13 that induce fibrogenesis in liver injury (56,69).

Both kupffer cells and HSCs express Toll-like receptors (TLR) as diagnostic receptors. The activation of TLR-4 increases chemokine secretion and stimulates HSCs, so that TGF-β can act on it (1,56,70). Perpetuation is the result of preservation of signals which lead to more increase in cytokine secretion and progression of extracellular matrix (ECM) synthesis (1).

There are several markers used as indicators of hepatic fibrosis. These markers include serum markers of liver function (AST, ALT), ECM synthesis (Collagens, glycoproteins, proteoglycans, hyaluronan, neo-epitopes (N-terminal pro-peptide of collagen type III (PIIINP)), fibrolytic processes (MMPs and TIMPs), ECM degradation (CO3-610, Co6-573), and fibrogenesis related cytokines (TGF-β1, CTGF, PDGF, TNF-α, IL-4, 6, 8, 18) (71) (Fig 2).

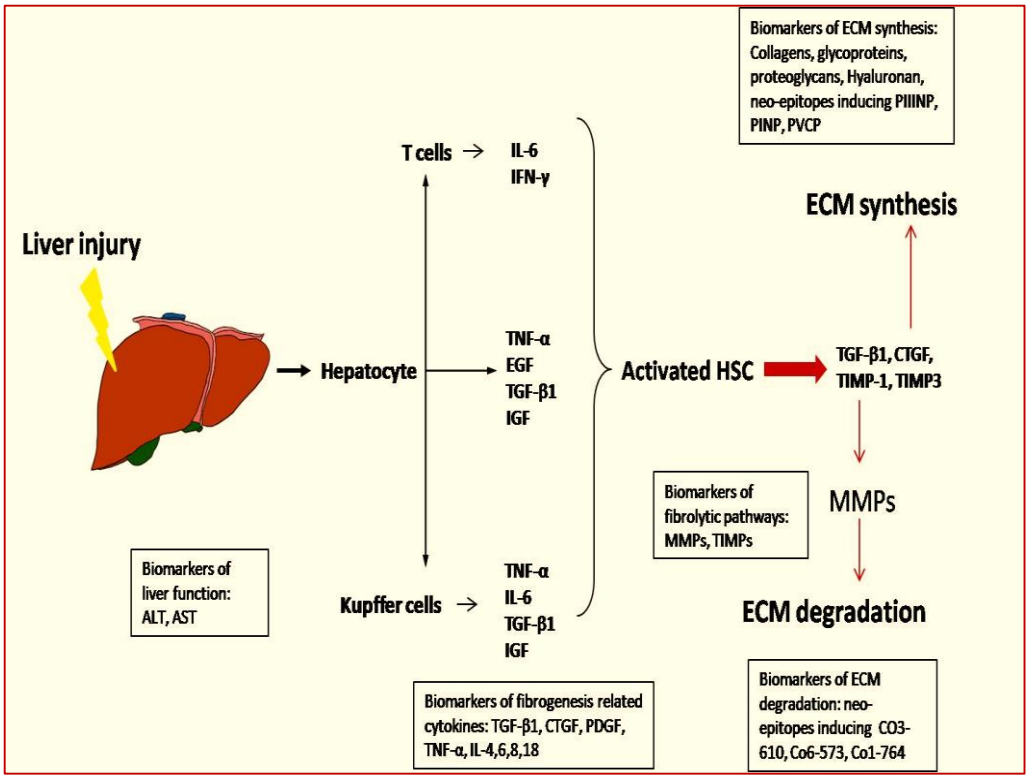

Figure 2. Mechanisms of hepatic fibrogenesis and possible molecular serum biomarkers. Some molecular serum biomarkers may reflect the pathogenesis of liver fibrosis: neo-epitopes, are related to basement membrane degradation; pro-collagen, is related to extracellular matrix (ECM) synthesis; MMPs and TIMPs are relate to ECM fibrolytic processes; ALT and AST are related to liver function and injury; other serum markers are fibrogenesis- related cytokines.

In the present, there is no standard cure for liver fibrosis. Although studies in animal models have showed the positive effects of plant compounds for preventing fibrosis progression, there is no evidence from the efficacy of these treatments in humans. The elimination of the causative agent is the most effective way to treat liver fibrosis. Meanwhile, effective antifibrotic remedial ways include down-regulating HSCs activation, neutralizing antiproliferative and fibrogenic responses of HSCs, increasing matrix destruction, increasing HSCs apoptosis and cytokine therapy (56). On the other hand, side effects of synthetic drugs are main reason to investigate medicinal plants on the treatment of fibrosis There are many active compounds which can be effective in the treatment of hepatic fibrosis. These compounds include silymarin, armepavine, plumbagin, total saponins, Puerarin rhein, glycyrrhetinic acid, ginseng, crocin and crocetin, resveratrol, curcumin, and salvianolic acid that have been widely studied. Table 1 shows the medicinal plants on the treatment of fibrosis together with their molecular mechanisms.

Silymarin is an extract gained from the seeds of milk thistle plant (*Silybum marianum*) (21,72). It is used clinically for the treatment of liver diseases as "hepato- protective" agent (21,73). Because of Silymarin significantly scavenge free radicals, it has antifibrotic properties in the liver (21,74). It ameliorates liver fibrosis by restoring the level of α-smooth muscle actin (a-SMA) in

rats treated by CCl4 (21). a-SMA is a marker of hepatic stellate cells activation leading to liver fibrosis (75).

Armepavine is an active compound from *Nelumbo nucifera* (41). It is reported that armepavine has antioxidant or free radical scavenging activities (76,77). Armepavine is also able to improve liver fibrosis by down-regulating the expression of TNF-α and profibrogenic (TGF-β, TIMP-1, procollagen I) genes (41,76).

Plumbagin (5-hydroxy-2-methyl-1, 4-naphthoquinone) is extracted from the roots of plant *Plumbago zeylanica* L. (Plumbaginaceae). Plumbagin has biological activities, such as anti-inflammation, anti-cancer and anti-oxidant activity (34,78-80). It reduces phosphorylation of epidermal growth factor receptor (EGFR) in fibrotic liver, and as a result it reduces the activation of HSCs by targeting EGFR signaling pathway (34). It is reported that plumbagin reduces the expression of TNF-α and α-SMA degrades ECM in CCl4 injured rats (81).

Total saponins are the major component of plant *Taraphochlamys affinis.* Saponins possess anti-hepatitis B virus (HBV) outcome (28) and protective effects against hepatic fibrosis (82). In CCl4 induced rats, total saponins from *Rosa laevigata* Michx (RLTS) effectively decreased the expression of PDGF-β and the activation of Akt and p70. Saponins also reduce hepatic fibrosis by reduction of PDGF and attenuating hepatic stellate cell activation (20,82).

Puerarin is a C-glycoside compound in *Pueraria lobata* (35). In traditional medicine, *P. lobata* has been used in therapy the problems associated with liver injury (24,83). Puerarin acts as a strong antioxidative agent (24,84,85). In CCl4 induced rats, Puerarin decreased expression of B-cell lymphoma 2 mRNA. Consequently, it could also induce the recovery of hepatic injury and apoptosis in activated HSCs (35).

Rhein, is an active component of rhubarb (*Rheum officinale*) to treat chronic liver disease. Rhein has several actions including antioxidant and anti-inflammatory activities, inhibiting TGF-β1, and suppressing the activation of hepatic stellate cells (36).

Curcumin is a polyphenol found in the plant *Curcuma longa* (commonly known as turmeric). It has many activities such as hepatoprotective, antioxidant, antineoplastic, anti-bacterial, antiviral, antifungal, anti-inflammatory, antidiabetic, anticoagulant, activity (37,52). It affects fibrogenesis of liver cells by lowering TLR2 and TLR4 expression, inhibiting of HSC activation and reducing the a-SMA expression in CCl4 induced liver fibrosis (52).

Salvianolic acid (SA) is a phenolic compound extracted from *Salvia miltiorrhiza*. It possesses antioxidant property in liver microsomes and hepatocytes (83). SA decreases the expression of TGF-β1, a-SMA, TNF-a, IL-1b and inhibit inflammation in liver fibrosis (84,85).

Glycyrrhetinic acid (GA) is one of the derivatives of Glycyrrhizic acid. It is extracted from *Glycirrhiza glabra*. GA has anti-mutagenic, anti-inflammatory and anti-oxidant properties (39,86-88). GA can protect the liver from oxidative stress through activating the nuclear translocation of Nrf2 and increasing the activity of the antioxidant enzymes (39).

Ginseng is the roots of *Panax ginseng* (89,90). It decreases liver fibrosis by reducing a-SMA, TGF-b expression and inhibition of the HSCs activation (40).

Crocin and crocetin are important carotenoid glycosides in saffron (is identified as Zaa'fran). Crocin is an anti-oxidant compound that can heal liver damage induced by CCl4 (50,91,92). Treatment with saffron extract (crocin and crocetin) modulates the activities of anti-oxidant enzymes by increasing the levels of superoxide dismutase and catalase and reducing the level of malondialdehyde in CCl4 toxicity (50).

Resveratrol is a polyphenol. It is found in peanuts, skin of red grapes, berries and roots of Japanese knotwood (93). Resveratrol restrains oxidative damage and down-regulation of a-SMA, thus inhibits HSCs activation to obstruct liver fibrosis (49).

Conclusions

The present study explains some herbal medicines that can be effective for liver injuries. Herbal products have several properties such as anti-inflammatory, anti-oxidant, and fibrogenesis that can protect liver against unfavorable conditions. Side effects of synthetic drugs have limited the use of them for treating liver fibrosis. Therefore, herbal products can be considered as an alternative therapeutic strategy, since they have traditionally treated many diseases. Despite effective role of medicinal

plants in treating liver fibrosis, there was no adequate evidence supporting the clinical efficacy herbal products for treating liver fibrosis. In this regard, active molecules must be isolated from plants and tested in cellular and molecular levels. Besides, using animal model and in the next step clinical trials will be able to increase accuracy and precision of the findings.

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Conflict of Interests

The authors have no conflict of interests.

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مقاله مروری

نقش داروهای گیاهی در فیبروز کبد: شواهد چیست؟

مریم برقی[۱]، عصمت عالم زاده [۲،۳*]

۱. گروه بیوشیمی، دانشکده دامپزشکی، دانشگاه شیراز، شیراز، ایران
۲. مرکز تحقیقات سلولی و مولکولی، دانشگاه علوم پزشکی بیرجند، بیرجند، ایران
۳. گروه بیوتکنولوژی پزشکی، دانشکده پزشکی، دانشگاه علوم پزشکی بیرجند، بیرجند، ایران

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چکیده

بیماری فیبروز کبدی به دلیل تجمع بیش از حد پروتئین های ماتریکس خارج سلولی مانند کلاژن ایجاد می شود. فیبروز پیشرفته کبد به سیروز و در نهایت به سرطان کبد منجر می شود که جز موارد غیر قابل برگشت محسوب می شود. از این رو توجه به مراحل اولیه بیماری و درمان آن نقش اساسی در این بیماران دارد. داروهای مصنوعی که برای درمان بیماری های کبدی مورد استفاده قرار می گیرند، اغلب عوارض جانبی دارند و بنابراین، روش های درمانی باید به داروهای جایگزین، به ویژه داروهای گیاهی یا مشتقات آن‌ها تغییر یابد. امروزه داروهای جایگزین به دلیل قدرت درمانی طولانی مدت و عوارض جانبی ضعیف مورد توجه ویژه قرار گرفته اند. در این مقاله مروری، برخی از ترکیبات مشتق شده از گیاهان را که نقش مؤثری در بهبود آسیب‌های کبدی دارند، مورد بررسی قرار داده‌ایم. ما همچنین مکانیسم عملکرد این ترکیبات را تا حدودی ذکر کرده ایم. کارهای آینده باید روی مسیرهای مولکولی این ترکیبات متمرکز شود تا کاربردهای احتمالی این داروها مشخص شود.

کلمات کلیدی: داروهای گیاهی، فیبروز کبد، داروی جایگزین

***نویسنده مسئول: عصمت عالم زاده،** گروه بیوتکنولوژی پزشکی، دانشکده پزشکی، دانشگاه علوم پزشکی بیرجند، بیرجند، ایران
Email: esmat.alemzadeh@gmail.com
https://orcid.org/0000-0001-5287-4760