

REVIEW ARTICLE

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Herbal Medicines Used in Treatment of Nonalcoholic Fatty Liver Disease: A Mini-Review

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Abstract

Botanicals are used traditionally for treatment and prevention of the liver diseases. In the past decades, the use of herbal remedies for non-alcoholic fatty liver disease (NAFLD) has become more popular. This study was conducted to determine the efficacy of herbal medicines used for the treatment of NAFLD in clinical trials. This research was carried out by searching through the studies done on human beings, which have been reported from 1966 to Feb. 2016 and recorded in Cochrane Library, Google Scholar, Pub Med, and Scopus. Some medicinal herbs have been evaluated in human trials. A scientific evaluation of these manuscripts can give an insight into the ideas of the past: it might well be valuable in finding new data on the clinical use of the herbal medicines for the treatment of NAFLD and should lead to future opportunities to investigate their potential medicinal use. [GMJ.2016;5(3):107-113]

Keywords: Nonalcoholic Fatty Liver Disease; Clinical Trial; Herbal Medicine

Introduction

Non-alcoholic fatty liver disease (NAFLD) is characterized by fatty change of hepatocytes in patients with no history of overdrinking alcohol [1]. In a fatty liver, the weight of the deposited fat is greater than 5 percent of the liver's weight; or rather, the fat covers more than half of the hepatocytes. Up to now, 20-40% of the individuals suffer from NAFLD globally while its prevalence is estimated to be around 5% to 30% in Asia [2]. This figure is about 2.9% to 7.1% in Iranian people and meets 21.5% in southern Iran [3, 4]. Metabolic disorders such as insulin resistance are often observed in NAFLD patients. Epidemiologic information demonstrates that

the pathogenesis of fatty liver is related to age, sex, blood lipids, hypertension, obesity, and diabetes mellitus (DM). The NAFLD risk factors comprise of high fat and protein diet, male gender, the presence of metabolic syndrome characteristics, extra meals before sleep, and sedentary lifestyle. As a consequence of the modern lifestyle and the increasing senior population, incidence of fatty liver and the related diseases have been on the rise [4, 5].

The NAFLD is an important progressing liver damage epidemic. Its direct costs include medical and diagnostic expenses whereas the indirect costs are the loss of productivity and reduced health-related quality of life (HRQOL). The NAFLD can also lead to fi-

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brotic change and cirrhosis, which have no proven treatment [6-9]. The main challenge is how to manage successfully the fatty liver, a modern disease, which has become a serious problem for the gastroenterologists [5].

Treatment of liver diseases such as fatty liver, chronic hepatitis, and cirrhosis is not satisfactory enough. The effectiveness of routine medical treatments such as colchicine, interferon, corticosteroids, and penicillamine is not well documented besides the fact that there are side-effects. Both physicians and patients look forward to effective therapeutic agents with as little harm as possible. Medicinal plants potentially constitute such effective agents [10].

There is an increase in the use of complementary and alternative medicine (CAM) [11], especially herbal therapy, by the patients including those with liver diseases [12]. Complementary therapies, such as herbal drugs, have also been tested for treatment of NAFLD [10]. Different schools of CAM including Traditional Persian Medicine (TPM) and Traditional Chinese Medicine (TCM) have their own say in the disease treatment [13-15]. In recent years, many investigators have examined specific effects of the plants applied traditionally by native healers and herbalists for the treatment of liver diseases. Their usage has been reported to be efficacious for the treatment of a variety of diseases in addition to their ready availability, little side effects, and proven therapeutic mechanisms and benefits [16, 17].

Several hundred plants have been evaluated for a variety of liver diseases; however, only a small handful of them have been fully studied [10]. In this investigation, we aimed to review the human clinical studies comprehensively, reporting the effectiveness of medicinal plants in the treatment of NAFLD.

Search Strategies

PubMed, Scopus, Cochrane Library and Google Scholar databases were combed for English-language clinical trials from 1966 to Feb. 2016 that were to deal with simple medicinal plants used in the treatment of NAFLD. Three reviewers independently exam-

ined the abstracts of identified publications for relevance and extracted pertinent data from the selected reports. The search keywords were “NAFLD”, “medicinal plant”, “fatty liver”, “herb”, “herbal drugs”, and “traditional medicine”. Only publications with available abstracts were reviewed. All human clinical trials were included.

Herbal supplements and diet-based therapies are among the most common complementary remedies used for the treatment of NAFLD [18]. In recent studies, the use of plant extract/decoction, as well as polyherbal formulations, represent the traditional system of medicine, while extracting the active ingredients and their application for the treatment belongs to modern pharmacotherapy. Latest advances in the field of medicinal chemistry have led to the detection of active agents from the whole plant extract. Many phytochemicals have been screened for different human ailments a small number of such phytochemicals are even available in the drug market. Furthermore, synthesis of analogues of natural compounds has turned out to be the concentration point of (many) modern investigators—they have resulted in finding more effective compounds yet. The currently available herbal treatments used for the healing of NAFLD are listed in Table1.

Discussion

As a worldwide critical issue, prevention and treatment of NAFLD are vital for healthcare systems [28]. To date, there is no effective treatment for NAFLD, except for lifestyle modification and weight reduction which are considered as the first-line in disease approach [29]. Nevertheless, pharmacotherapy has also been considered by physicians for treatment [30].

Herbal medicine is a part and parcel of various brands of traditional medicine, extending back to a long time ago. Over the time, a variety of herbs were added to the database of medicine, which has been recorded in herbal pharmacopeia [31]. Indeed, many of new medicaments in common use have an herbal origin. Globally, about 25 percent of prescribed medications have at least one active ingredi-

Table 1. List of Herbal Medicines Used for the Treatment of NAFLD in Clinical Trials

Common name	Scientific name	Number of participants	Duration	Dose	Result	Reference
Green alga	<i>Chlorella vulgaris</i>	60	8 weeks	400 mg/day vitamin E plus four 300-mg tablets of <i>Chlorella vulgaris</i>	Weight, liver enzymes, FBS ^y and lipid profile decreased significantly	Ebrahimi-Mameghani, Aliashrafi <i>et al.</i> [17]
		76	3 months	<i>Chlorella vulgaris</i> extract (1200 mg/day) + metformin (750 mg/day) + vitamin E (200 mg/day) + or metformin (1250 mg/day) + vitamin E (200 mg/day)	Serum ALT [*] , AST [#] , TG [€] , uric acid, HbA1c, and insulin resistance index were all reduced in the <i>Chlorella</i> group significantly	Panahi <i>et al.</i> [18]
Green tea	<i>Camelia sinensis</i>	70	12 weeks	Green tea adjusted to 1,080 mg/700 ml or 200 mg/700 ml catechin content and green tea flavored beverage (0 mg/700 ml catechin content)	The high-density catechin treatment significantly decreased serum ALT levels and reduced urinary 8-isoprostane excretion as compared with the placebo and low-density catechin group	Sakata, Nakamura <i>et al.</i> [19]
Licorice	<i>Glycyrrhiza glabra L.</i>	66	2 months	one capsule containing 2 g aqueous licorice root extract per day	In the treatment group, the mean ALT and AST level decreased statistically significantly	Hajiaghahmohammadi, Ziaee <i>et al.</i> [20]

Continue in Next Page

Continue of Table 1. List of Herbal Medicines Used for the Treatment of NAFLD in Clinical Trials

Chamber bitter	<i>Phyllanthus urinaria</i>	60	24 weeks	400 mg of chamber bitter together with inactive ingredients of microcrystalline cellulose, hydroxypropylmethylcellulose and magnesium stearate	there was no significant difference in the changes in AST, FBS and lipid profile between the two groups The mean serum ALT levels in the silymarin group decreased. ALT normalization (ALT < 40) was observed in 52% of patients in the silymarin-treated group. AST normalization (AST < 40) was observed in 62% of cases in the silymarin-treated group.	Wong, Wong et al. [21]
Silymarin	<i>silybum marianum</i>	100	24 weeks	280 mg of silymarin	BMI [‡] , TG, Chol [‡] , ALT, AST, LDL [‡] , and FBS after treatment decreased compared to baseline but were not statistically significant.	Hashemi, Hajiani et al. [22]
Cumin	<i>cuminum cyminum L.</i>	100	6 months	cumin capsule (25 mg saponin) thrice [before main meals daily]	In the treatment group, the mean serum levels of ALT and AST decreased, which was statistically significant compared to the control group.	Shavakhi, Toriki et al. [23]
Barberry	<i>Berberis Vulgaris L.</i>	80	3 months	750 mg of barberry extract every day	In the cinnamon group, the mean serum levels of ALT and AST, gamma glutamine transpeptidase, and high-sensitivity C-reactive protein decreased which was statistically significant in contrast to the control group.	Iloon Kashkooli, Najafi et al. [24]
Cinnamon	<i>Cinnamomum zeylanicum</i>	50	12 weeks	1500 mg cinnamon daily		Askari et al. [25]

* ALT: Alanine aminotransferase, #AST: Aspartate aminotransferase, [‡]BMI: Body mass index, [‡]Col: Cholesterol, [‡]FBS: Fasting Blood Sugar, [‡]TG: Triglycerides, [‡]LDL: Low-density lipoprotein

ent of herbal source [32].

The TPM with its dynamic treasure of novel medicinal plants has introduced various options for gastrointestinal system ailments, ranging from prevention to treatment fields [33, 34]; in this regard, liver—as a vital organ—has a fundamental position.

According to our search, few human studies are focusing on this field. As demonstrated in Table 1, in most studies the effect of herbal drugs has been evaluated by changes in the level of Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), and the body mass index (BMI); however, there are no adequate data regarding histopathological improvement in these patients. Some clinical trials on medicinal plants showed changes in serum lipids, insulin resistance, and plasma glucose levels, too.

The mechanism of action for these medicinal plants is not crystal-clear; yet, some of them (such as *Chlorella vulgaris* and *silybum marianum*) have proven to be effective in decreasing plasma lipid [24, 35]. Decrease in AST was observed in patients with alcoholic liver disease on silymarin comparing to placebo but, it was not attributable to NAFLD patients [36]. Such property could explain their therapeutic role in treating NAFLD patients.

The mechanism of action for *Berberis vulgaris* effect on NAFLD patients was similar to the latter result in decreasing plasma total cholesterol and triglycerides but, different in liver enzymes. Barberry decreased ALT, AST, and weight in the case group vs. control group significantly which fact could clarify its effectiveness unmistakably [2].

On the other hand, the anti-oxidative stress effects of some medicinal plants such as silymarin and green tea [37, 38] have a crucial role in the treatment of other accompanied ailments such as DM and cardiovascular diseases (CVD). Green tea enriched with catechines, a major component of its extract, reduces body fat composition and CVD risks, too [39, 40]. Green alga and cinnamon consumption could also result in a decline in FBS and lipid profile [19, 20, 27]. Healing of these common concomitant diseases could justify the effectiveness of such plants.

It is not to be forgotten that there are cases where herbal medication does not come inef-

fective, as, for instance, in the case of chamber bitter [23]. It is not exactly clear to us why in this one case the herbal medication does not act effectively. Unfortunately, there is only one report which has assessed the histological changes by herbal drugs; the rest of the studies have evaluated only the effects of medicinal plants on metabolic profile or radiological changes after treatment.

As the decrease in fibrosis level is the main goal of previous treatments, we cannot assess the exact effect of these medicinal plants on the therapeutic outcome. Thus, need felt for further double-blind randomized controlled trials with an adequate number(s) of NAFLD patients, assessing the histopathological changes of the liver with long-term follow-up.

Our review of current literature revealed that only a small number of medicinal plants showed adverse effects. However, the safety profile of any herbal product could be determined after rigorous evaluations and long-term follow-up.

Conclusion

Medicinal plants have proven to be effective for the correction of the metabolic profile of NAFLD patients, with few reports of adverse effects. Nonetheless, few studies have addressed the effect of herbal remedies on the histopathological characteristics of patients with NAFLD. The evaluating merits of herbals for the management of NAFLD could be the main objective of future research. Well-designed clinical trials with adequate participants and histopathological investigations are needed to evaluate both efficacy and safety of these natural products.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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