

Natural Products for the Treatment of Hepatitis C

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ABSTRACT

Hepatitis C is a global health concern and is one of the main causes of liver disease, which generates a lot of social and economic burden. There is currently no epidemic vaccine to prevent this infection. Although current treatment is effective, it is not available in many countries. Therefore, discovery and identification of a new inexpensive drug to provide easy access is a priority. For this purpose, the scientific databases of PubMed, Scopus, Google Scholar and NAPRALERT were used. The findings showed that camel milk and medicinal herbs such as *Acacia nilotica* can be effective for treatment of hepatitis C.

Key words: Hepatitis C, Natural products, Herbal products, Animal products, Camel milk

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INTRODUCTION

Acute viral hepatitis is an infection that primarily affects the liver. Hepatitis C can be either acute or chronic but tend to be chronic in most cases. Hepatitis C is now the main cause of hepatitis after blood transfusions. Hepatitis C, in addition to the blood transfusion virus, is transmitted through injection of intravenous drugs. The risk of infection in haemodialysis centres increases. Donor blood screening is the most important method for controlling and preventing hepatitis C. In order to prevent hepatitis C, blood donation should be checked for ALT and anti-HBc markers. The most sensitive test for detecting hepatitis C is HCV-RNA. Sexual transmission risk is about 5%. Hepatitis C causes forty percent of cases of chronic liver disease and is the most common indication of liver

transplantation. Most cases of mortality and morbidity are in the first 20 years after infection. Factors that are involved in the progression of chronic hepatitis include: age of disease onset, duration of infection, immune weakness, drinking too much alcohol and etc. [1]. Due to frequent hepatitis C virus mutations, there is currently no epidemic vaccine to prevent this infection. Although current treatment [2] is effective, it is not available in many countries. Therefore, discovery and identification of a new inexpensive drug to provide easy access is a priority.

MATERIALS AND METHODS

Data collection was conducted from reputable scientific databases such as PubMed, Google Scholar, Scopus and NAPRALERT during April 2008 to July 2018 which was based on keywords such as Hepatitis C, natural products, herbal and animal products, camel milk. Searching for articles was done in both English and Persian without time limitations.

RESULTS

Hepatitis C treatment with natural products (herbs)

Herbs have several biological compounds. For example, flavonoids [3], tripenoids, lignoids [4], alkaloids, and phenolic acids [5] show antiviral properties. Flavonoids are natural phenolic compounds found primarily in fruits, vegetables, cereals, skin, roots, stems, flowers, tea and wine [6]. Most anti-bacterial, anti-tumor, anti-parasitic and antiviral activities associated with flavonoids are due to their antioxidant activity [7]. Studies have shown that antiviral activity of flavonoids is often against herpes simplex virus, respiratory viral virus, parainfluenza virus and adenovirus [8]. There are many herbal antiviral and protective effects against viruses like influenza virus, type 2 herpes simplex virus [9], immune deficiency virus [10,11], hepatitis B virus [12], and severe acute respiratory syndrome [13].

About 30 plant species belonging to 24 families have been reported for the treatment of jaundice and hepatitis. In all cases, the oral route has been used. For example, hexanoic and alcoholic extracts from the fruits of *Phyllanthus Emblica*, *Tamarindus indica* and *Punica granatum* are antimicrobial, while the leaves and roots of *Justicia adhatoda*, the whole *Cichorium intybus* plant, *Morus Alba* and *Myrsine africana* fruits do not show any antimicrobial activity [14]. The aqueous extract of *Tamarindus indica* fruit has antimicrobial activity, while the whole *Beta procumbens* plant has no antimicrobial activity [15]. Prajapati et al. showed *Rhizopus chinensis* has antibacterial, antiviral and antifungal activity [16].

It seems that there are many species of medicinal herbs elsewhere that have not been reported yet [17]. Researches also indicated the antiviral activity of the extract obtained from the leaves of *Warscewiczia coccinea* in inhibiting the proliferation of HBV (Hepatitis B virus) and HIV-1 (human immunodeficiency virus-type 1) [18]. Several herbal extracts of herbs have been successful in controlling the hepatitis virus. Extract of *Acacia nilotica* [19], *Solanum nigrum* [20] and *Phyllanthus amarus* [21] showed HCV inhibition and *Phyllanthus urinaria* extract successfully inhibited HBV proliferation [22]. Other studies on the antiviral effects of the *Embelia schimperi* extract revealed two important antibiotics, Amblyin and 5-o-methylumbelliferone which are protease inhibitors in HCV disease [23]. *Chamaecyparis lawsoniana* is a plant that has a phenolic compound and can suppress herpes simplex virus (HSV). Scientists found that *Mimosa pudica* and *Paederia foetida* extract had antiproliferative effects on porcine epithelial cells, while *Kaempferia galanga* extracts had more antiproliferative effect on the proliferation of porcine macrophages. The survival and growth of cytotoxic effects on porcine epithelial (CLAB) and porcine macrophage cell lines (PoM2) infected with HEV (hepatitis E virus) increased after treatment with *Mimosa pudica* (1.39 fold) and *Kaempferia galanga* (1.54 fold) compared to untreated cells. Therefore, it can be concluded that the extracts of *Mimosa pudica* and *Kaempferia galanga* are able to prevent the binding of these viruses to their specific receptors and thus

contribute to prolonging cell life. It is not yet clear how the extract of these plants inhibits the virus. Scientists believe that the extracts of these plants are likely to reduce the expression of different receptors on the surface of the cells which are responsible for the interconnection and internalization of the particles of the virus. More studies are needed to understand the antiviral effects of these plants on the binding of the virus to specific cell-receptors [24]. Another study showed that the *Fumaria parviflora L* reduces the liver lesions induced by carbon tetrachloride [25].

The Silymarin (milk thistle) medicinal extract also has hepatoprotective properties and has been used in many ways for treating disorders and diseases of the liver and gastrointestinal tract during the years [26,27]. The herbal medicine containing multiple flavonoids protects the liver against a variety of toxication such as Amanita, Alcohol, Acetaminophen, and Galactosamine and carbon tetrachloride [28-30].

The use of aqueous and alcoholic extracts of different plants can reduce the effects of liver damage induced by carbon tetrachloride injection and improve the liver tissue. In liver damage caused by carbon tetrachloride dissolved in olive oil, an injection of *Ginkgo gobiloba* extract prevented necrosis and liver fibrosis. The protective effect of this plant is achieved by reducing the liver marker enzymes and lipid peroxidation [31]. In another study, it was found that the aqueous and alcoholic extract of *Capparis decidua* stems has a protective effect on the liver against the hepatotoxicity of carbon tetrachloride dissolved in paraffin oil in rats. This study showed that compounds such as alkaloids, flavonoids, tannins, sterols, saponin, cyanogenic glycosides and coumarins which are the main components of the extract can prevent liver tissue damage against carbon tetrachloride [32]. The study of the aqueous and ethanolic extracts of the *Vitex trifolia* leaves showed that the plant eliminates the toxic effects of CCL4 (carbon tetrachloride). The mechanism is reducing the total bilirubin and liver enzymes caused by liver tissue damage. Histopathologic studies confirm these results [33]. The phytochemical analysis of the methanolic extract of Carissa and Papaya leaves indicate compounds such as flavonoids, tannins, alkaloids, flobatanins, tripenoids, coumarins, and glycosides in the extract of this plant. These compounds inhibit liver damage through antioxidant activity and membrane stability [34]. The leaves and petioles of the Panirac plant were analyzed to determine the type and amount of compounds such as fatty acids, mineral elements, total flavonoid, mucilage, tannin and nitrate. The findings showed that linolenic acid, palmitic acid, and oleic acid comprise more than 82% of total fatty acids of the leaf and petioles of this plant. Chromatography and mass spectrometry of methanol extract revealed that 2-methoxy-4-vinylphenol is the main compound in the extract of this plant which is an effective ingredient in the antioxidant activity and free radicals removal [35]. Other medicinal herbs such as Saffron [36], Pune leaf [37], Physalis root [38], Piquantus [39], Caricampa [40],

Silicobin [41] and Phycoccus [42] can reduce the damaging effects of carbon tetrachloride in hepatocytes and improve the liver tissue by help of different chemical compounds and antioxidant activities, as well as removing free radicals. These plant also contains tannins, leucoanthocyanins, anthocyanins, mucilages [24,43], phenols, flavonoids, carotenoids and alkaloids which increase the antioxidant enzymes such as superoxide dismutase, catalase and glutathione peroxidase [44]. Since antioxidants are able to protect the liver against damage by reducing lipid peroxidation and hepatocytic necrosis, it is thought that the cause of the reduction in the number of necrotic cells is the presence of antioxidants in the extract of the cucumber plant [45].

Animal products for the treatment of hepatitis C

Studies have shown that camel milk is used to treat hepatitis C. The camel's milk immunoglobulin has no light chain and is known as a nanobody. Nanobody, due to the ability to detect unusual and hidden antigens as well as the ability to convert to multi-treatment therapeutic proteins has been considered as a good tool in designing novel immunotherapy strategies for the treatment of cancer, inflammatory and infectious diseases. These immunoglobulins can be transmitted through the milk [46-48]. On the other hand, in human studies, the effects of lactoferrin extracted from cattle and camel milk have been evaluated as a combination therapy with standard hepatitis C drugs. All studies confirm the positive effect of camel milk lactoferrin in treating hepatitis [49-51]. The consumption of camel milk in patients with chronic hepatitis B enhance the immune system and increase the serum level of interferon gamma and some other cytokines. It also prevents the virus from replication, thereby increasing the rate of healing in patients with chronic hepatitis B [52]. Several studies with the examination of pathologic images and laboratory markers and biochemical parameters demonstrate the protective and therapeutic effects of camel milk on the liver of rats contaminated by carbon tetrachloride, alcohol and paracetamol. Laboratory tests in this regard indicate improvement in the treatment of the disease along with the repair of the liver tissue. It seems that taking camel milk in liver toxicity can play an effective role in detoxification [53-55].

Researches showed that the special fat of camel milk is a liver healer and has beneficial effects for patients with chronic hepatitis [52]. It is said the relatively high concentration of ascorbic acid in camel milk may improve liver function [56]. Some studies have shown that lactoferrin in camel milk significantly inhibits hepatitis C genotype 4 infection by preventing the virus from entering the cells [57]. In addition, lactoferrin in camel milk is much more potent than lactoferrin in human milk and buffalo for anti-viral activity and can even destroy schistosoma mansoni [51,58] with antiparasitic measures. Mal et al. reported that camel milk antibodies are strong and selective viral enzyme inhibitors. In addition, immunoglobulins boost the immune system

against viral and bacterial infections such as tuberculosis [59].

A human study done in 2009 on 44 patients with chronic hepatitis B showed that camel milk consumption resulted in a significant reduction in ALT (Alanine aminotransferase) and HbsAg (Hepatitis B surface antigen) and HBV DNA (Deoxyribonucleic acid of Hepatitis B virus) will be negative 54 and 90 percent respectively compared to the control group patients [60].

Effects of camel milk in hepatitis C were evaluated in 2014 in Pakistan. In this study, 500 cc of camel milk was administered to patients for two and half months daily and the blood sample was tested every fifteen days. The results showed a decrease in the hepatic enzymes [61].

In the study of El-Fakharany et al., the therapeutic effects of lactoferrin extracted from camel, cattle and sheep milk on HepG2 (HepG2 is an immortalized cell line consisting of human liver carcinoma cell) infected with hepatitis C virus in a cell culture medium were investigated and the results showed that the strongest therapeutic effect was observed in genotypes a4 [62]. In a study by Redwan et al. the effect of pure lactoferrin extracted from camel milk in a cell culture medium infected with hepatitis C virus genotype 4 was investigated and its anti-viral effect was confirmed after seven days [51]. In the study of Redwan et al., the effects of polyclonal/antibody of camel milk on human hepatoma cell line (Huh-7) in a cell culture medium infected with hepatitis C virus were investigated and destruction of viral synthesized peptides as well as inhibition of virus growth were reported, while human immunoglobulins (IgG) have not had this effect [63]. In another study, EL-Fakharany et al., reported significant lactoferrin antiviral effects extracted from camel milk on peripheral blood mononuclear white blood cells (PBMcs) and Human hepatoma (HepG2) infected cells with HCV (hepatitis c virus) [64]. According to Morin et al. the therapeutic effects of lactoferrin vary according to their concentration in camel milk (from 95 to 250 mg/dL). The iron-saturated lactoferrin (from the second week of camel lactation) prevents microbial growth in the intestines and participates in the immune system. The camel's milk supposedly contains lactoferrin much more than herbivorous mammals (cattle, sheep and goats) [65].

CONCLUSION

The use of natural products and the study of scientific evidence that result from them can lead to inexpensive and low-cost treatments. However, the use of herbs and camel milk bioactive components in the treatment of hepatitis, as outlined in this article requires research and studies. It seems that the use of natural and classical products in the treatment of disease together may provide new solutions and more favourable results in the treatment of hepatitis C virus. Further studies and stronger evidence are needed to prove the effect of the use of natural products.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this study.

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