In this issue of our newsletter we review the treatment of liver disease with botanical agents, based on an article published in the Journal of Restorative Medicine.

As suggested in the article abstract, liver disease has “become a global health problem associated with the increased prevalence of harmful chemicals in the environment and the use of pharmaceuticals known to have detrimental effects on liver function as well as alcohol abuse”.

The article reviews the usage of some specific medicinal herbs which have proven to be of significant benefit for liver disease and the herbs mention some that you would be familiar with (such as Turmeric, Milk Thistle) but also some that you may not be familiar with because their origin and main usage patterns occur in Ayurvedic Medicine, Chinese Medicine and in SE Asia (such as Guduchi, Amla, Bupleurum, Madder, Andrographis and Azadirachta indica.

This list includes two of our personal favourites for this specific application, namely Tinospora cordifolia (Guduchi, an Ayurvedic Medicine adaptogen) as well as Bupleurum which is used extensively in Chinese Medicine for this and other applications.

Like almost all medicinal herbs, the specific ones discussed in this article target the indicated application (liver disease) but also provide many additional benefits.

For example, let’s look at our two personal favourites: Guduchi and Bupleurum.

**Here is a quick outline of the many health benefits provided by these two medicinal herbs:**

**Guduchi – Health Benefits**

- Allergies and symptoms of hay fever
- Arthritis and inflammation
- Chronic skin disorders such as psoriasis or eczema
- Gout and rheumatic disorders
- Hepatitis and jaundice (helps protect the liver from exposure to toxins)
- Immune system enhancement
- Preventing colds and flu
- Reducing the side effects of chemotherapy drugs
- It acts as a bitter tonic and this gives it the ability to act as an appetizer
- Guduchi is a febrifuge
- It has a significant action on improving liver function by destroying toxins; it is considered highly effective in treating liver damage due to hepatitis or jaundice
- Guduchi has a marked action as an aphrodisiac
- It increases sexual potency
- It is used to treat digestive problems such as hyperacidity, abdominal pain, colitis, vomiting and loss of appetite
- External application of Guduchi paste is said to be effective in treating chronic skin disorders such as eczema and psoriasis and also helps to impart a healthy glow to skin.
- Recent studies have shown it to have great value as an adaptogen.
- Guduchi has also shown promising results as an anti-diabetic agent.
- Animal studies have found that extracts of the plant are capable of inhibiting the action of some of the enzymes involved in increasing blood glucose levels.

Information sourced from the Chopra Center and The Health Site

**Bupleurum – Health Benefits**

- Bupleurum demonstrates antiviral properties. Bupleurum has been shown to inactivate enveloped viruses including measles and herpes, but had no effect on non-enveloped viruses such as polio.
- Bupleurum may be helpful in the inactivation of certain hepatitis viruses.
- Bupleurum acts as an anti-inflammatory.
- The saikosaponins found in bupleurum stimulate corticosteroid production, thus increasing the anti-inflammatory effects.
- Saikosaponins can inhibit the growth of liver cancer cells.
- Saikosaponins have been found to help lower plasma cholesterol.
- Capable of shielding the liver from damage, saikosaponins demonstrated marked hepatoprotective activity in several animal models.
- Shown to expedite the healing of an injured liver, saikosaponins increase hepatic protein synthesis both in vitro and in vivo.
- Bupleurum herb is traditionally used as an herbal tonic to bring about improved functioning of the liver, studies done in Japan confirmed the protective effect of Bupleurum root extract to liver.
- Bupleurum root extract is also used to treat gastrointestinal problems and hemorrhoids.
- Bupleurum also used to promote perspiration by aiding the body to rush blood to the surface, beneficial in clearing fever, flu and inflammation due to infection.
- Bupleurum is also used to treat brain disorders, and female reproductive problems.
- Bupleurum is also being considered and studied for its anti-cancer properties.

Information sourced from Medical Health Guide and Liver Support.com
Biotics offers a number of formulations for the liver and gall bladder:

- **Livotrit Plus** (Livotrit includes some of the ingredients mentioned in this article: Guduchi, Andrographis and Milk Thistle)
- **Beta-TCP**
- **Beta Plus**
- **Cytozyme-LV (Liver)**
- **MCS CANADA (Metabolic Clearing Support)**
- **Mg-Zyme**
- **NAC (N-Acetyl-L-Cystine)**
- **Nutri-Clear**
- **Lecithin 3X (formally: Phosphatidylcholine)**
- **Super Phosphozyme Liquid**

Following is the article on the treatment of liver disease with botanical agents.

Regards,

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The Treatment of Liver Disease with Botanical Agents

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ABSTRACT

Traditional herbal medicine has gained increasing attention as alternative therapy for the treatment of liver disease, which has become a global health problem associated with the increased prevalence of harmful chemicals in the environment and the use of pharmaceuticals known to have detrimental effects on liver function as well as alcohol abuse. Herbal derived medicines such as Turmeric (*Curcuma longa*), Guduchi (*Tinospora cordifolia*), Amla (*Emblica officinalis*), Milk Thistle (*Silybum marianum*), Madder (*Rubia tinctorum*), Andrographis (*Andrographis paniculata*), Bupleurum and Azadirachta indica have shown hepatoprotective and regenerative effects mainly associated with their antioxidant and anti-inflammatory properties, and they have been used as adjunctive or stand alone agents for the treatment of several conditions affecting liver function. *Curcuma longa*, a culinary spice known as Turmeric, and *Bupleurum* have been used in traditional medicine for the treatment of liver disease.
The active component of *Curcuma* is the flavonoid curcumin, which has been researched extensively for its beneficial effects on several liver diseases. The active components of *Bupleurum* are the saikosaponins, which have hepatoprotective effects and have shown activity against the hepatitis B virus. The hepatoprotective effects of *Silybum* are thought to be mediated by its constituent flavonolignans, which are commercially available in a crude extract labeled silymarin and a semipurified flavonoid, *Silibinin*. The efficacy of these hepatoprotective herbs is determined by routine testing of liver enzymes including AST, ALT, ALP and bilirubin. Although some side effects have been reported, these have not been validated by clinical studies, and the safety of these supplements has been demonstrated when used at the appropriate doses.

Keywords

- Hepatoprotective effect,
- Liver disease,
- AST,
- ALT,
- Herbal medicine

AARM REFERENCE REVIEWS

These are AARM reference reviews in which clinicians can obtain a quick overview of understanding with respect to how herbs, nutrients, and hormones can be used effectively in clinical practice. The dosages recommended are based on therapeutic results. Side effects that have not been seen in clinical experience or found in clinical studies but only been theorized have been identified and depicted as Unsubstantiated Theoretical Concerns.

Since many nutrients and herbs on the market have not gone through double-blind studies but have been used extensively in clinical settings for hundreds, and for some thousands of years, these reference reviews have attempted to give a unified opinion on how to use these herbs effectively. The opinions expressed are from different professors and experts in the field of nutritional and botanical medicine. Some information is based on personal opinions and cannot be quantified as fact. However, if clinicians only restricted themselves to what is fully proven by double-blind studies, the art of healing and restoring health with nutrients and herbs would be lost.

CLINICAL IMPLICATIONS

Liver disorders are a major global health problem, and factors negatively affecting liver function include pollution, exposure to environmental chemicals, drug use (prescription and non-prescription), and alcohol abuse, as well as hormones and additives tainting the food supply.
Curcuma (Turmeric), Tinospora, Emblica, Silybum (Milk Thistle), Rubia, Andrographis, and other herbal therapeutic agents have been shown to protect the liver from various hepatotoxic substances. Many of the hepatoprotective and regenerative benefits of these herbs appear to be due to antioxidant and anti-inflammatory effects.

KEY HERBS DISCUSSED

Turmeric (Curcuma longa), Guduchi (Tinospora cordifolia), Amla (Emblica officinalis) Milk Thistle (Silybum marianum), Madder (Rubia tinctorum), Andrographis (Andrographis paniculata), Bupleurum and Azadirachta indica

PRIMARY INDICATIONS

Elevated liver enzymes, chemical/toxic exposure and chemical sensitivities, conditions affecting liver function, detoxification, prevention of toxicity due to specific pharmaceuticals, Gilbert’s syndrome, jaundice, and as adjunctive treatment for hepatitis or liver cancer

ADJUNCTIVE OR STAND-ALONE TREATMENT

Adjunctive or Stand-Alone

DOSE OF BIOACTIVE CONSTITUENTS

Milk Thistle Whole Plant Extract 900 mg daily, containing a minimum of 520 mg of silymarin daily, Synergistic Herbal Formula: Milk Thistle (Silybum) extract, Guduchi (Tinospora), Amla (Emblica), Rubia (Rubia), Andrographis (Andrographis), Yellow Dock (Rumex), Oregon Grape Root (Mahonia), Burdock (Arctium), Schizandra (Schisandra), Globe Artichoke (Cynara).

BIOACTIVE CONSTITUENTS

Silybum: Silymarin, Flavonolignans
Curcuma: Curcumin
Bupleurum species: Saikosaponin
Tinospora: Dioterpenes, Arabinogalactan polysaccharides
Emblica (Phyllanthus): Flavonoids
Azadirachta indica: Flavonoids
Rubia: Rubiadin, Anthocyanins, Anthroquinones
**Andrographis**: Andrographolide, Bicyclic diterpenoid lactones

**CAPSULE DOSE**

**Silybum**: 175-600 mg *per day* (110 mg silymarin)

**Curcuma**: Up to 8 g *per day* in divided doses for 18 months

**Bupleurum species**: 400-500 mg *twice per day*

**Tinospora**: 400-800 mg *twice per day*

**Emblica**: 400-800 mg *three times per day*

**Azadirachta indica**: 500-1000 mg *twice per day*

**Rubia**: 400-500 mg *twice per day*

**Andrographis**: 400-800 mg *twice per day*

**SIDE EFFECTS AND CAUTIONS**

To monitor efficacy of these supplements clinicians suggest the following tests to routinely monitor progress. These tests include AST, ALT, ALP, and bilirubin. In high doses, effects can be seen within a week except for *Rubia*. These herbs are safe when used appropriately. *Bupleurum*, Neem and *Andrographis* and standardized *Curcumin* in high doses can cause gastric irritation in people with sensitive stomachs. *Andrographis* in high very doses can cause gastrointestinal distress, and loss of appetite. *Andrographis* should not be taken in pregnancy.

**THEORETICAL UNSUBSTANTIATED SIDE EFFECTS**

*Neem* and *Tinospora cordifolia* theoretically may increase the risk of hypoglycemia. *Bupleurum* theoretically interferes with interferon-alpha. *Silybum* theoretically should be used with caution in patients with gallstones or a bile duct obstruction or in those with stomach ulcers or excess stomach acid or with blood thinners. However, no clinical or scientific evidence has validated any of these concerns.

**COMMENTS**

Avoiding exposure to known hepatotoxins (*e.g.*, cleaners such as dry-cleaning fluid, alcohol-based cleaners, pesticides, synthetic chemicals and solvents) should be encouraged. Milk Thistle standardized to 80% is actually a misnomer.
Milk Thistle extract marketed in the US as 80% *Silymarin* was based on an inaccurate UV test to artificially increase the lab value of *Silymarin*. The true *Silymarin* 80% content actually is reflected by HPLC testing as 53%.

**DISCUSSION**

Herbal medicine offers a safe and supportive therapeutic option to improve liver function. In this era where humans are environmentally bombarded by harmful chemicals (*e.g.*, in air and food), the use of liver-strengthening herbs may assist the body to process and detoxify the effects of some toxic environmental substances. In addition to environmental toxins, pharmaceuticals can induce liver toxicity; pharmaceutical drugs known to induce hepatotoxic effects include nitrosamine, acetominophen, adriamycin, carbon tetrachloride, hexane, benzene, and aflatoxin.

*In vivo* and human clinical placebo controlled studies conducted to demonstrate the effectiveness of detoxifying herbs have evaluated the effectiveness of the herbs on blood concentrations of the liver enzymes (*e.g.*, AST, ALT, GGT) found at time of initiation of treatment to post-therapeutic intervention with herbal dosing to assess efficacy of the treatment regimen.

**THE USE OF *SILYBUM MARIANUM* TO PROMOTE LIVER HEALTH**

In the herbal tradition, *Silybum marianum* is probably the most well-known herb for promoting liver health, and it has been the subject of numerous investigations demonstrating its hepatoprotective effects. *Silymarin*, a collection of at least seven known flavonolignans, and *Silibinin* (one of the primary flavonoids) are both credited with the herb’s hepatoprotective effects. Other flavonolignans found within *Silymarin* include *Silybin* A and B, *Silychristin*, *Silydianin*, and *Isosilybin* A and B.

Studies with animal models have shown *Silybum* and its individual flavonolignans to positively affect liver metabolism. The hepatoprotective effect of *Silybum* has been so well documented that some European and U.S. hospitals utilize it intravenously as an antidote for acute liver toxicity due to ingestion of poisonous mushrooms. *Silymarin* displays immunomodulatory effects on virally-induced liver inflammation. Certain *Silymarin* constituents are also reported to have anti-carcinogenic effects.

Animal models of nonalcoholic-related steatohepatitis suggest *Silybum* therapy may be beneficial based on improvements of elevated liver enzymes, gene expression assays, and other biochemical and immunological markers. Further, animal studies suggest that *Silybum* protects the liver from aflatoxins and carbon tetrachloride.
In a Phase I clinical trial, *Silybin* A and B were used on patients with noncirrhotic hepatitis C. *Silybum* therapy showed promise in treating hepatitis C, and was safe and well tolerated. Another human clinical trial in hepatitis C patients found that *Silymarin* therapy inhibited the proliferation of pro-inflammatory cytokines from infected T cells.

*Silymarin* also has iron-chelating effects. A randomized, double-blind, placebo-controlled clinical trial demonstrated the positive effects of *Silymarin* and desferoxamine in patients with beta-thalassemia major. After three months, *Silymarin* and desferoxamine were more effective than either desferoxamine alone or placebo in reducing serum ferritin, lowering the iron overload, and normalizing elevated liver enzymes.

In a clinical trial of acute hepatitis patients, *Silybum* therapy eliminated the symptoms of elevated bilirubin (*i.e.*, jaundice, icterus, and dark urine) more quickly than in the placebo group.

**THE USE OF CURCUMA LONGA TO PROMOTE LIVER HEALTH**

*Curcuma longa* (a member of the Zingiberaceae family), a culinary spice known as Turmeric, gives Indian curries their typical bright-yellow color. *Curcuma* is traditionally used in Chinese and Indian herbal medicine for treating liver disease. It has been extensively studied, not only for its beneficial effects on the liver, but for its systemic immune, anti-inflammatory, and antioxidant effects. *Curcuma* has been studied as an alternative therapy for patients with both liver and digestive diseases; *Curcumin* is a flavonoid that has been credited with powerful antioxidant and anti-carcinogenic effects.

Animals pretreated with curcumin showed less damage to the liver when exposed to carbon tetrachloride, a powerful hepatotoxin. Curcumin has also been shown to protect the liver from benzene toxicity. Additionally, the co-administration of curcumin and aflatoxin was shown to decrease LDH and ALT when elevated, and Curcumin was shown to protect liver cells from ethanol and acetaminophen toxicity.

Other research investigations have shown that Curcumin can inhibit NF-κB which, in turn, upregulates pro-inflammatory and profibrotic cytokines. Curcumin reduces the ability of alcohol, iron overload, biliary stasis, carbon tetrachloride, and adriamycin (doxorubicin) to damage the liver. Further, studies have demonstrated the ability of curcumin to provide protection against decreased liver function due to viral hepatitis by enhancing both synthesis and protective levels of hepatocellular proteins.

In a variety of inflammatory conditions, hepatic stellate cells are known to undergo transformation that ultimately leads to liver fibrosis. *Curcuma* and *Curcumin* have been shown to help a diseased liver recover normal hepatic stellate cells. *Curcumin* also stimulates the gallbladder to excrete bile at a faster rate, and may be beneficial in the treatment of biliary colic and bile stones/sludge.
While studies have shown that Curcumin has powerful systemic effects, it is also poorly absorbed. Curcumin—with the added black pepper alkaloid (Piperine), or Curcumin—with phosphatidylcholine (Lecithin) is much more bioavailable.\textsuperscript{35,36}

It has been shown to act as a chemosensitizer and radiosensitizer for tumor cells, while at the same time protecting healthy cells from harmful effects to the liver from chemotherapy and radiation.\textsuperscript{37} Future clinical studies may further delineate a role for Curcumin as adjunctive therapy for the treatment of cancer.

**BUPLEURUM AND THE TREATMENT OF LIVER DISEASE**

In traditional Chinese medicine, Chai hu (*Bupleurum*) is an important herb in the treatment of liver disease. *Bupleurum* yields a number of pharmacologically active compounds, though the most relevant for the treatment of liver disease are the saikosaponins, a type of steroidal saponin glycoside.\textsuperscript{38} Similar to the previously described herbs, the saikosaponins have been shown to be protective in animal models of hepatotoxicity. Pre-treatment of rats with saikosaponin-d was able to protect the liver from carbon tetrachloride-induced cellular damage.\textsuperscript{39} In this study, the herbal extract appeared to inhibit lipid peroxidation. Other researchers have demonstrated saikosaponin-d to be a potent inhibitor of collagen deposition in carbon tetrachloride-induced liver fibrosis.\textsuperscript{40} Moreover, the extract normalized markers of liver inflammation (e.g., TGF-\(\beta\)-1).

Saikosaponin-c is active against the hepatitis B virus (HBV).\textsuperscript{41} This is due in part to the ability of Saikosaponin-c to inhibit cells from releasing the hepatitis B antigen and to impair HBV DNA replication.\textsuperscript{42} On the other hand, Saikosaponin-d exhibits a proapoptotic effect on cancer cell lines by affecting the cellular production of p53, nuclear factor kB, and the Fas/Fas ligand.\textsuperscript{43} A possible adverse interaction between *Bupleurum* and interferon-alpha has been suggested; therefore, concurrent use with interferon-alpha is contraindicated.

**THE USE OF TINOSPORA TO PROMOTE LIVER HEALTH**

*Tinospora cordifolia* (a member of the *Menispermaceae* family) is an Ayurvedic herb known as Guduchi. *Tinospora cordifolia* and *Phyllanthus emblica* (also known as *Emblica officinalis*, and a member of the *Phyllanthaceae* family) are often used in combination in Ayurvedic medicine for the treatment of liver diseases.

*Tinospora* was shown to support normal metabolism and has been shown to inhibit carbon tetrachloride-induced liver toxicity.\textsuperscript{44-46} In guinea pigs treated for tuberculosis with a regimen known to cause hepatotoxicity, *Tinospora* prevented elevation of the liver enzymes, serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), as well as alkaline phosphatase.\textsuperscript{47} In another animal study, three medications commonly known to induce liver damage were given to rats for 90 days; *Tinospora* and *Phyllanthus* were simultaneously
administered in the experimental rat group which showed fewer histological changes typically associated with hepatotoxicity.48

A human clinical trial examined the use of Tinospora in 30 patients with jaundice due to malignant obstruction and associated sepsis and immunosuppression.49 Patients were randomized into two groups; both groups received vitamin K, antibiotics, and biliary drainage. One group received Tinospora and the other group received placebo for 3 weeks after institution of the biliary drainage. At the end of the 3 week period, biochemical and immunologic assessments were made. Hepatic function was similar in both groups, but the group receiving Tinospora displayed better immune function. While 50% of the placebo group experienced septicemia, none occurred in the treatment group. Only 40% of the patients not receiving Tinospora survived surgical biliary drainage, while over 92% of the patients receiving Tinospora survived the surgical drainage.49

THE USE OF EMBLICA OFFICINALIS TO PROMOTE LIVER HEALTH

Emblica officinalis (also known as Amla or Indian Gooseberry) produces bright-yellow fruits that are high in flavonoids and Vitamin C. Studies have shown Emblica upregulates mitochondrial activity which in turn affects potassium channels in the liver.50 Emblica has been shown to protect the liver from various hepatotoxins including arsenic and Nitrosamine and inhibits systemic oxidative stress due to renal disease.51–53

In studies, protection against the hepatotoxic effects of Nitrosamine (a known hepatotoxin and mutagen) by Emblica has been demonstrated.54

Further, Emblica may be able to reverse histological changes and assist the liver in repairing and recovering from early pathological manifestations. Similar hepatoprotective effects have been demonstrated with Emblica following exposure to hexane compounds.55 Hexane typically damages the liver, elevating peroxides and depleting the liver of glutathione and dehydrogenase-detoxifying enzymes. Research studies have shown Emblica to prevent cellular changes in the liver and promote antioxidant detoxification in the liver.56,57 Emblica improved lipid metabolism and protein expression, suggesting utility in prevention of oxidative stress from long-standing hyperlipidemia.58

AZADIRACHTA INDICA AND THE TREATMENT OF LIVER DISEASE

The leaves of Azadirachta indica, a traditional Indian plant from the Meliaceae (or mahogany) family, have been used in Ayurvedic medicine to treat liver ailments as well as parasitic, fungal, and microbial infections. Marketed as Neem, the plant is also a natural insecticide against aphids and common agricultural pests.59–61

Azadirachta enhances lipid and protein processing in the liver. Extracts have been shown to protect the liver from phenobarbital62 and nitrosamine toxicity.63 Azadirachta appears to have a systemic chemoprotective effect by aiding the liver’s metabolism of hormones.64
Prophylactic treatment of Swiss albino mice with a Neem leaf preparation was shown to slow the growth of Ehrlich’s carcinoma without causing any associated hepatotoxicity as evidenced by normal liver enzymes (AST and ALT) and hepatic histology.65

A wide array of active compounds have been identified in Azadirachta and at least 140 have been shown to have potential medicinal and therapeutic effects thus far.66 The insecticidal and pesticidal compounds include compounds called Azadirachtins.67 Many studies and many commercial products mention Neem “oil” which is extracted from the seeds of Azadirachta and known to contain a complex mixture of compounds including high amounts of terpenoids, limonoids and volatile sulphur containing compounds.68 One study reported Neem oil to affect aspartate transferase (AST), alanine transferase (ALT) and alkaline-phosphatase (ALPK) enzyme systems in insects.69

THE USE OF RUBIA TINCTORUM TO PROMOTE LIVER HEALTH

Rubia tinctorum or Manjishta is a member of the Rubiaceae family found in Southeast Asia. In the West, it is known as Madder (or Red Madder) due to its brilliant red color and use as a plant dye. Its high anthocyanin content (similar to the compounds in berries and red wine credited with antioxidant effects) provides the red dye’s color.70 One such anthocyanin, Rubiadin, may protect the liver from carbon tetrachloride toxicity as evidenced by the normalization of elevated liver enzymes and the recovery of depleted glutathione enzymes.71 Purpurin, a pigmented anthraquinone, has been shown to inhibit mutagenic effects on the liver following exposure to several of the substances in the Ames mutagenicity panel.72 Activity against the hepatitis B virus has been attributed to quinone compounds in Rubia roots.73

Toxicology studies have found that Rubia is hepatotoxic in rats following chronic daily exposure of ≥300 mg per kilogram of body weight (equivalent to a dose of 48.4 mg/kg in humans).74 However, the traditional amount of Madder in herbal formulas is substantially less. While Madder dye may have human carcinogenic effects with long-term exposure,75 small doses appear to have hepatoprotective effects.77 78

THE USE OF ANDROGRAPHIS PANICULATA TO LIVER HEALTH

Much of the hepatoprotective activity of Andro-graphis has been credited to andrographolide (a bicyclic diterpenoid lactone).74 Like other hepatoprotective plants, Andrographis acts on hepatocyte organelles.74 In animal models, Andrographis has been investigated as a therapeutic agent in treating liver cancer.75 Studies have shown that Andrographis improves general glycogenolysis, glucose transport, and metabolism by liver enzymes. In turn, this suggests that Andrographis supports basic liver metabolism and may help the liver recover when these functions are impaired.75

Andrographis paniculata (a member of the Acanthaceae family) may reduce the tendency of liver cells to lyse in the presence of high cytokine levels.76
Liver-specific inflammatory conditions and indeed most general inflammatory conditions result from excessive cytokine release. While cytokines are an important component of a healthy immune response, in some allergic (and inflammatory and immunologic) conditions, the release of cytokines contributes to tissue destruction. Likewise, in some liver abnormalities, cytokines trigger apoptosis of healthy hepatocytes and contribute to the loss of liver function.

While *Andrographis* may aid in the prevention of inappropriate apoptosis of functional liver cells, it may also enhance the apoptotic effect of chemotherapeutic agents on cancerous cells in the liver. In one study, *Andrographis* enhanced the efficacy of 5-fluorouracil against hepatocarcinoma, suggesting a role for its adjunctive use with chemotherapy. *Andrographis* also supports high levels of glutathione in the liver, one of the liver’s mechanisms for self-protection. For example, glutathione depletion is believed to be the main mechanism of acetaminophen-induced hepatotoxicity. Furthermore, *Andrographis* has been shown to aid in protection of the liver from the damaging and inflammatory effects of hexane, cyclophosphamide and carbon tetrachloride.

**SUMMARY**

In conclusion, the herbs described in this review have been shown to offer hepatoprotective and detoxifying benefits via a variety of mechanisms and have been used in combination for their synergistic effect.

Symptomatic improvement has been observed in patients with allergies (e.g., chemical sensitivities) on a treatment regimen of these herbs. This improvement may be due to improved clearance of the allergenic substances. Likewise, a reduction in liver and digestive symptoms (as well as improvement in liver function test results) may occur as early as one week following initiation of herbal treatment.

Many of the hepatoprotective and regenerative benefits of these herbs appear to be due to antioxidant and anti-inflammatory effects. A published case study suggested that use of the herbs described in this review reduced liver metastatic tumors in a patient diagnosed with melanoma. Only *Rubia* has been shown to have a dosage restriction and possible toxicity.

The studies cited in this review suggest that these herbs may particularly benefit individuals with liver function abnormalities due to such causes as chemical-induced hepatotoxicity, hepatitis, and cirrhotic degeneration.
DISCLOSURE OF INTERESTS

Dr. Saunders reports personal fees related to employment or seeing patients from CCNM, the Dundas Naturopathic Centre, and from Beaumont Health Systems, Troy Hospital, MI, outside the submitted work. Dr. Winston reports personal fees from Herbalist & Alchemist, Inc, outside the submitted work. Dr. Stansbury and Dr. Zampieron have nothing to disclose.

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