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Herbs for Enhancing Phase I/II Hepatic Detoxification

Schisandra

Schisandra chinensis (*Schizandra chinensis*) fruit is indicated in traditional Chinese medicine (TCM) to arrest discharges, replenish *qi*, quiet the spirit, promote fluid secretion, tonify the *Kidney* and nourish the *Liver*. It is used for chronic cough, nocturnal emission, spermatorrhoea, frequent urination, protracted diarrhoea, night sweats, wasting disorder, palpitations and insomnia.[1,2] Schisandra has been used in the Far East as a tonic, particularly in fatigue. Indigenous Siberians used dried Schisandra berries to combat fatigue during their hunting trips.[3,4]

Major constituents of Schisandra fruit are the dibenzocyclooctene lignans (approx. 2% by weight) including schisandrin and gomisin A.[5]

Schisandra and/or the lignans from Schisandra have demonstrated antioxidant, hepatoprotective activities and enhancement of phase I/II hepatic metabolism *in vivo* when administered orally.[6-8]

The mechanism of action of the hepatoprotective activity is likely to include:[6,9,10]

- antioxidant activity within the liver,
- facilitation of glutathione regeneration,
- stabilisation of the membrane of the hepatic parenchymal cells,
- inhibition of the activation of the hepatotoxin and the binding of its resultant metabolites to liver microsomes,
- induction of heat shock proteins.

Administration of Schisandra over a 2-week period improved liver enzymes in poorly performing sport horses.[11] A single dose of Schisandra improved race times, reduced heart rate and facilitated recovery in race and show jump horses.[12,13]

Clinical Studies

Schisandra fruit given as an oral liquid (10 g/day) for 60 days significantly increased the superoxide dismutase (SOD) activity in serum compared with that of the control group.[14]

Clinical studies in China indicate that Schisandra has lowered elevated liver enzymes in patients with hepatitis.[15] Schisandra has been evaluated in uncontrolled trials and used in Russia as an adaptogen, for example to increase endurance and mental and physical efficiency.[16,17]

St Mary's Thistle

For centuries *Silybum marianum* (previously *Carduus marianus*) has been recommended in Europe for the treatment of liver disorders,[18] and more recently for jaundice, gallstones, gallbladder colic, hepatitis and haemorrhoids.[19] In the traditional medicine of Germany, the fruit is regarded as a cholagogue, hepatoprotective and stimulant of portal circulation.[18] In addition to many of these indications St Mary's Thistle was also used by the Eclectic physicians for splenic, hepatic and renal congestion.[20] It is also used in other countries such as Pakistan and Bulgaria for liver diseases.[21,22]

St Mary's Thistle fruit contains an active, lipophilic, flavanolignan mixture known as silymarin, which consists mainly of three isomers: silybin, silychristin and silydianin. Most standardised extracts contain 70–80% of silymarin.[23,24]

St Mary's Thistle has well documented hepatoprotective activity and possible mechanisms of action may include:[25,26]

- increasing protein synthesis in the hepatocyte,
- inhibiting lipid peroxide formation,
- scavenging of free radicals,
- stabilising of cell membranes.

Standardised extract of St Mary's Thistle beneficially affected lactation performance in dairy cows during peripartum (a period during which animals may develop subclinical fatty liver).[27]

Clinical Studies

Antioxidant activity has been demonstrated in healthy volunteers and patients with chronic renal disease (858 mg/day of silymarin),[28,29] patients with alcoholic liver disease/cirrhosis including those with diabetes (most common dose: 420 mg/day of silymarin) and patients exposed to psychotropic drugs (800 mg/day of

silymarin).[30-37] Parameters measured included total plasma antioxidant capacity, lipid peroxidation, glutathione (in plasma and erythrocytes), serum glutathione peroxidase, malondialdehyde (erythrocytes), (erythrocytes) and SOD expression (erythrocytes and/or lymphocytes).

A survey of European hospital-based specialists in gastroenterology/hepatology in 1992 found that 13–18% of them considered using silymarin for patients with alcoholic fatty liver, alcoholic fibrosis, alcoholic hepatitis or alcoholic cirrhosis.[25]

A 1999 review concluded that silymarin (280–800 mg/day) may improve the clinical course and survival rates from acute and chronic hepatitis, and drug-, toxin- and alcohol-induced hepatitis,[38] although later reviews and a 2005 meta-analysis have not confirmed these results. However, a significant beneficial effect in improving bilirubin and gamma-glutamyltransferase (GGT) was found. Rigorously designed clinical trials involving patients with well-defined liver disease are required.[25]

Rosemary Leaf

Rosmarinus officinalis leaf contains an essential oil, phenolic diterpenes (including carnosol and carnosic acid), rosmarinic acid, flavonoids and triterpenoids. Rosemary leaf has been traditionally used for the treatment of flatulent dyspepsia, poor digestion, headache, depression, chronic circulatory weakness and to stimulate the mind.[6]

In European herbal medicine Rosemary is well regarded for improvement of hepatic and biliary function and in dyspeptic conditions.[39,40] Culpeper recommended it for 'cold' diseases of the liver.[41]

Pharmacological Activity

Rosemary has a strong *in vitro* antioxidant activity in saturated fats,[42] which is unusual as most antioxidant plant extracts and phytochemicals demonstrate activity in aqueous systems. The strong antioxidative activity of Rosemary is attributable to the phenolic diterpenes,[43] about 90% of the activity is attributed to carnosol and carnosic acid.[44]

Rosemary extract and/or constituents have inhibited lipid peroxidation, scavenged free radicals, protected against oxidative damage to DNA and inhibited DNA strand breaking *in vitro*.[6,45] Dietary intake of Rosemary extract inhibited adduct formation and reduced tumour incidence in an experimental model.[46] Rosemary extracts have demonstrated hepatoprotective activity *in vivo* (by oral route).[47,48] The activity was attributed to the antioxidant phenolic compounds.[47]

Water-soluble extract of Rosemary (containing rosmarinic acid, flavones and monoterpenes but no phenolic diterpenes) induced phase I enzymes and phase II enzymes *in vivo*.[49] The phase II enzymes glutathione-S-transferase and quinone reductase were increased in another *in vivo* study by oral administration of (undefined) Rosemary extracts.[50] In both studies the extract had greater activity than isolated constituents administered by the same route.[49,50] Another *in vivo* study of similar design found that essential oil induced phase I enzymes, dichloromethane extract containing phenolic diterpenes induced phase II enzymes, and the water-soluble extract (without phenolic diterpenes) enhanced both.[51]

Full spectrum extracts are likely to give the best overall activity, considering the traditional use of the herb and the results of animal studies.

Synergistic Formulation

These herbs would complement each other in a very potent formulation providing primarily enhancement of phase I/II hepatic detoxification but also antioxidant and hepatoprotective activity.

Indications

- Toxin overload or poor hepatic detoxification function.
- Conditions associated with poor liver detoxification such as headache, allergies, skin disorders, fatigue, nausea, food intolerance, constipation.
- Exposure to environmental or chemical toxins including patients regularly taking prescribed medications or ingesting alcohol.
- Hormonal disorders (in both men and women).
- Poor liver function, liver damage, hepatitis.

Cautions and Contraindications

Schisandra is contraindicated in pregnancy, except at birth. According to TCM Schisandra is contraindicated in the early stages of cough or rash and in excess heat patterns.

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