**Picrorhiza kurroa**

**Introduction**

Picrorhiza kurroa is a well-known herb in the Ayurvedic system of medicine and has traditionally been used to treat disorders of the liver and upper respiratory tract, reduce fevers, and to treat dyspepsia, chronic diarrhea, and scorpion sting. It is a small perennial herb from the Scrophulariaceae family, found in the Himalayan region growing at elevations of 3,000-5,000 meters. Picrorhiza kurroa has a long, creeping rootstock that is bitter in taste, and grows in rock crevices and moist, sandy soil. The leaves of the plant are flat, oval, and sharply serrated. The flowers, which appear June through August, are white or pale purple and borne on a tall spike; manual harvesting of the plant takes place October through December. The active constituents are obtained from the root and rhizomes. The plant is self-regenerating but unregulated over-harvesting has caused it to be threatened to near extinction. Current research on Picrorhiza kurroa has focused on its hepatoprotective, anticholestatic, antioxidant, and immune-modulating activity.

**Active Constituents**

Kutkin is the active principal of Picrorhiza kurroa and is comprised of kutkoside and the iridoid glycoside picrosides I, II, and III. Other identified active constituents are apocynin, drosin, and nine cucurbitacin glycosides. Apocynin is a catechol that has been shown to inhibit neutrophil oxidative burst in addition to being a powerful anti-inflammatory agent, while the curcubitacins have been shown to be highly cytotoxic and possess antitumor effects.

**Mechanisms of Action**

The hepatoprotective action of Picrorhiza kurroa is not fully understood but may be attributed to Picrorhiza’s ability to inhibit the generation of oxygen anions and to scavenge free radicals. Picrorhiza’s antioxidant effect has been shown to be similar to that of superoxide dismutase, metal-ion chelators, and xanthine oxidase inhibitors. In rats infected with malaria, Picrorhiza restored depleted glutathione levels, thereby enhancing detoxification and antioxidation, and helping maintain a normal oxidation-reduction balance. In this same animal model, Picrorhiza also demonstrated an anti-lipid peroxidative effect. Like silymarin, Picrorhiza has been shown to stimulate liver regeneration in rats, possibly via stimulation of nucleic acid and protein synthesis. Picrorhiza’s anti-inflammatory action is attributed to the apocynin constituent, which has been shown to have potent anti-inflammatory properties in addition to inhibiting oxidative burst in neutrophils. Although the mechanism is unclear,
animal studies indicate Picrorhiza’s constituents exhibit a strong anticholestatic activity against a variety of liver-toxic substances, appearing to be even more potent than silymarin. Picrorhiza also exhibits a dose-dependent choleretic activity, evidenced by an increase in bile salts and acids, and bile flow.  

**Clinical Indications**

**Hepatic Insult and Damage**

Numerous animal studies, primarily in rats, have demonstrated that the active constituents of *Picrorhiza kurroa* are effective at preventing liver toxicity and the subsequent biochemical changes caused by numerous toxic agents. Hepatocytes damaged by exposure to galactosamine, thioacetamide, and carbon tetrachloride were incubated with Picrorhiza constituents. A concentration-dependent restorative effect was observed in regard to normal hepatocyte function. A similar effect was seen when 25 mg/kg/day oral Picrorhiza extract was administered to rats poisoned by aflatoxin B1 exposure. *Picrorhiza kurroa* significantly prevented the biochemical changes induced by aflatoxin B1 extract, when given at a dose of 3-12 mg/kg orally for 45 days, was also shown to be effective in reversing ethanol-induced liver damage in rats. In an animal model of hepatic ischemia, rats given Picrorhiza orally at 12 mg/kg daily for 7 days, prior to induced ischemia, demonstrated improved hepatocyte glycogen preservation and reduced apoptosis, compared to control animals. Picrorhiza principals have also shown to be effective in treating Amanita mushroom poisoning in an *in vivo* animal model. An *in vitro* study demonstrated Picrorhiza’s antioxidant activity by subjecting human Glioma and Hep 3B cells to a hypoxic state. Picrorhiza treatment reduced the cellular damage cause by hypoxia, indicating Picrorhiza constituents may protect against hypoxia/reoxygenation-induced injuries.

**Viral Hepatitis**

Studies indicate Picrorhiza extracts may be of therapeutic value in treating viral hepatitis. An *in vitro* study investigated anti-hepatitis B-like activity of Picrorhiza and found it to have promising anti-hepatitis B surface antigen activity. In a randomized, double-blind, placebo-controlled trial of 33 patients diagnosed with acute viral hepatitis, 375 mg Picrorhiza root powder was given three times daily for two weeks. The treatment group was comprised of 15 patients; the remaining 18 subjects acted as controls and received placebo. Bilirubin, SGOT, and SGPT values were significantly lower in the treatment group, and the time required for bilirubin values to drop to 2.5 mg% was 27.4 days in the treatment group versus 75.9 days for the placebo group.

**Asthma/Allergy**

*In vivo* studies of bronchial obstruction indicate that the drosin constituent of *Picrorhiza kurroa* prevented allergen- and platelet activating factor-induced bronchial obstruction when given to guinea pigs via inhalant and oral routes. *In vitro* histamine release was also inhibited by the plant extract. Picrorhiza extract given orally at 25 mg/kg to mice and rats resulted in a concentration-dependent decrease in mast cell degranulation. However, induced bronchospasm was not prevented, indicating a lack of direct post-synaptic histamine receptor blocking activity.

**Dosage and Toxicity**

Picrorhiza is not readily water-soluble and is therefore not usually taken as a tea. While it is ethanol soluble, the bitter taste makes tinctures unpalatable, so it is therefore usually administered as a standardized (4% kutkin) encapsulated powder extract. Typical adult dosage is 400 to 1500 mg/day, with dosages up to 3.5 g/day sometimes being recommended for fevers. Picrorhiza root extracts are
widely used in India with no adverse effects having been reported. The LD$_{50}$ of kutkin is greater than 2600 mg/kg in rats with no data available for humans.\textsuperscript{23}

References