



Monograph

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.^{1,2}

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.^{3,4} Apocynin is a catechol that has been shown to inhibit neutrophil oxidative burst in addition to being a powerful anti-inflammatory agent,⁵ while the cucurbitacins have been shown to be highly cytotoxic and possess antitumor effects.⁶

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.⁷ *Picrorhiza*'s antioxidant effect has been shown to be similar to that of superoxide dismutase, metal-ion chelators, and xanthine oxidase inhibitors.⁸ In rats infected with malaria, *Picrorhiza* restored depleted glutathione levels, thereby enhancing detoxification and antioxidation, and helping maintain a normal oxidation-reduction balance.⁹ In this same animal model, *Picrorhiza* also demonstrated an anti-lipid peroxidative effect.¹⁰ Like silymarin, *Picrorhiza* has been shown to stimulate liver regeneration in rats, possibly via stimulation of nucleic acid and protein synthesis.¹¹ *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.⁵ 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 choleric activity, evidenced by an increase in bile salts and acids, and bile flow.¹²

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, thiocetamide, and carbon tetrachloride were incubated with Picrorhiza constituents. A concentration-dependent restorative effect was observed in regard to normal hepatocyte function.¹³ 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 B1.¹⁴ Picrorhiza 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.¹⁵ 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.¹⁶ Picrorhiza principals have also shown to be effective in treating Amanita mushroom poisoning in an *in vivo* animal model.¹⁷ 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.¹⁸

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.¹⁹ 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.²⁰

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.²¹ 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.²²

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 LD₅₀ of kutkin is greater than 2600 mg/kg in rats with no data available for humans.²³

References

- Atal CK, Sharma ML, Kaul A, Khajuria A. Immunomodulating agents of plant origin. I: preliminary screening. *J Ethnopharmacol* 1986;18:133-141.
- Subedi BP. Plant profile: Kutki (*Picrorhiza scrophulariiflora*). *Himalayan Bioresources* 2000;4.
- Weinges K, Kloss P, Henkels WD. Natural products from medicinal plants. XVII. picroside-II, a new 6-vanilloyl-catapol from *Picrorhiza kuroa* Royle and Benth. *Justus Liebig's Ann Chem* 1972;759:173-182. [Article in German]
- Stuppner H, Wagner H. New cucurbitacin glycosides from *Picrorhiza kurroa*. *Planta Med* 1989;55:559-563.
- Simons JM, 't Hart BA, Ip Vai Ching TR, et al. Metabolic activation of natural phenols into selective oxidative burst agonists by activated human neutrophils. *Free Radic Biol Med* 1990;8:251-258.
- Stuppner H, Wagner H. New cucurbitacin glycosides from *Picrorhiza kurroa*. *Planta Medica* 1989;55:559.
- Russo A, Izzo AA, Cardile V, et al. Indian medicinal plants as antiradicals and DNA cleavage protectors. *Phytomedicine* 2001;8:125-132.
- Chander R, Kapoor NK, Dhawan BN. Picroliv, picroside-I and kutkoside from *Picrorhiza kurroa* are scavengers of superoxide anions. *Biochem Pharmacol* 1992;44:180-183.
- Chander R, Kapoor NK, Dhawan BN. Effect of picroliv on glutathione metabolism in liver and brain of *Mastomys natalensis* infected with *Plasmodium berghei*. *Indian J Exp Biol* 1992;30:711-714.
- Chander R, Singh K, Visen PK, et al. Picroliv prevents oxidation in serum lipoprotein lipids of *Mastomys coucha* infected with *Plasmodium berghei*. *Indian J Exp Biol* 1998;36:371-374.
- Singh V, Kapoor NK, Dhawan BN. Effect of picroliv on protein and nucleic acid synthesis. *Indian J Exp Biol* 1992;30:68-69.
- Shukla B, Visen PK, Patnaik GK, et al. Choleric effect of picroliv, the hepatoprotective principle of *Picrorhiza kurroa*. *Planta Med* 1991;57:29-33.
- Visen PK, Saraswat B, Dhawan BN. Curative effect of picroliv on primary cultured rat hepatocytes against different hepatotoxins: an *in vitro* study. *J Pharmacol Toxicol Methods* 1998;40:173-179.
- Rastogi R, Srivastava AK, Rastogi AK. Biochemical changes induced in liver and serum aflatoxin B1-treated male wistar rats: preventive effect of picroliv. *Pharmacol Toxicol* 2001;88:53-58.
- Saraswat B, Visen PK, Patnaik GK, Dhawan BN. *Ex vivo* and *in vivo* investigations of picroliv from *Picrorhiza kurroa* in an alcohol intoxication model in rats. *J Ethnopharmacol* 1999;66:263-269.
- Singh AK, Mani H, Seth P. Picroliv preconditioning protects the rat liver against ischemia-reperfusion injury. *Eur J Pharmacol* 2000;395:229-239.
- Dwivedi Y, Rastogi R, Garg NK, et al. Effects of picroliv, the active principle of *Picrorhiza kurroa*, on biochemical changes in rat liver poisoned by *Amanita phalloides*. *Chung Kuo Yao Li Hsueh Pao* 1992;13:197-200.
- Gaddipati JP, Madhavan S, Sidhu GS, et al. Picroliv – a natural product protects cells and regulates the gene expression during hypoxia/reoxygenation. *Mol Cell Biochem* 1999;194:271-281.
- Mehrotra R, Rawat S, Kulshreshtha DK, et al. *In vitro* studies on the effect of certain natural products against hepatitis B virus. *Indian J Med Res* 1990;92:133-138.
- Vaidya AB, Antarkar DS, Doshi JC, et al. *Picrorhiza kurroa* (Kutaki) Royle ex Benth as a hepatoprotective agent – experimental and clinical studies. *J Postgrad Med* 1996;42:105-108.
- Dorsch W, Wagner H. New antiasthmatic drugs from traditional medicine? *Int Arch Allergy Appl Immunol* 1991;94:262-265.
- Baruah CC, Gupta PP, Nath A, et al. Anti-allergic and anti-anaphylactic activity of picroliv – a standardised iridoid glycoside fraction of *Picrorhiza kurroa*. *Pharmacol Res* 1998;38:487-492.
- Annual Report, Regional Research Laboratory, Council for Scientific and Industrial Research, India. 1989-1990.