Kutkins- A Review of Chemistry and Pharmacology

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Abstract

Kutkins are group of pharmacologically active compounds present in Picrorhiza kurroa Royle (Scrophulariaceae). Picrorhiza kurroa is traditionally known as kutki and has intense bitter taste. In Ayurveda Picrorhiza kurroa is a reputed remedy for the treatment of liver diseases. The chemical composition of the Picrorhiza has been studied and active constituents are group of iridoid glycosides known as picrosides and kutkosides. The mechanism of action of kutkins appears to the same as that of silymarin (active constituent and hepatoprotective constituent of Silybum marianum). Studies have shown that kutkins are more potent than silymarin as far as hepatoprotective activity is concerned.

Keywords: Hepatoprotective/Picrorhiza kurroa/Kutkin**.**

Introduction:

Picrorhiza kurroa Royle is a distinguished medicinal herb of Ayurveda. It has been described under the group of bitter drugs. Picrorhiza kurroa is a small perennial herb that grows in hilly parts of India particular in Himalayas between 3000 and 5000 meters. It is an established herbal remedy for variety of disease ranging from indigestion to hepatitis. Modern clinical studies have confirmed the efficacy and safety of Picrorhiza kurroa for the treatment of liver disease. The roots and rhizomes are used in medicinally important parts. Powder, decoction, infusion, confection, and alcoholic extract of the drug are prescribed in Ayurveda and Homeopathy.

Botany:

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.

Chemistry:

The chemistry of Picrorhiza kurroa is complex. The active constituent is known kutkin and is a mixture of:

A. Kutkoside

B. Picroside.

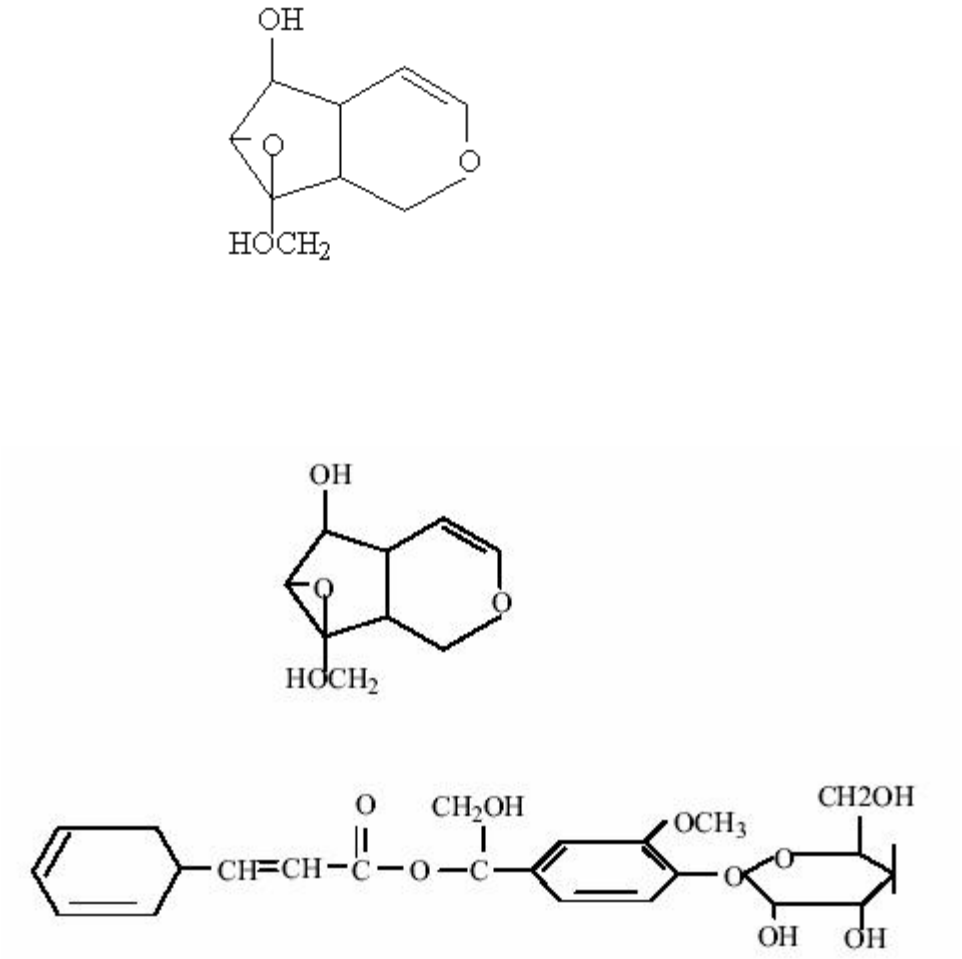
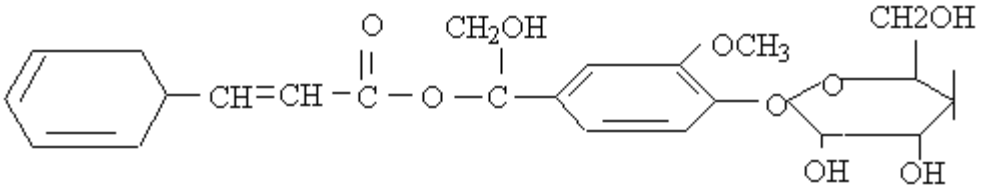


Fig 1. Structure of Kutkins(Kutkosides and Picrosides).



Picrosides are iridoid glycosides and have been further divided into picrosides I, II, and III.

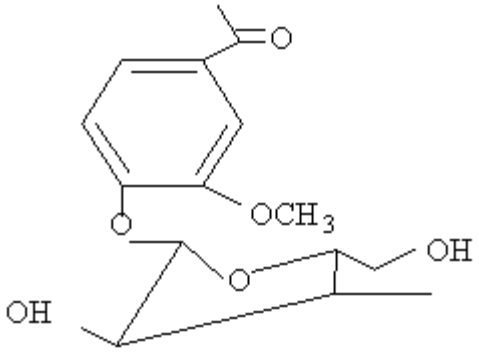


Fig 3. Structure of Androsin

Other constituents are apocynin, andorsin, and cucurbitacin glycosides.

Pharmacologically, Kutkin (Picrosides and kutkosides) has hepatoproptective activity. Apocynin is a potent NADPH oxidase inhibitor and has anti-oxidant and anti-inflammatory activity. Androsin has anti-asthmatic effect.

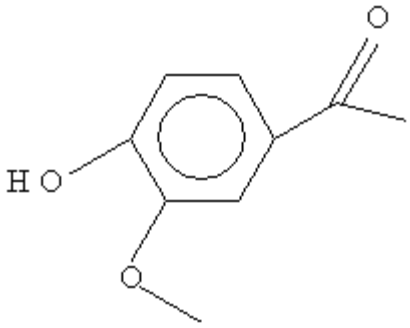


Fig 2: Structure of Apocynin

A colorimetric method has been developed for the analysis of the total iridoid content of the rhizomes of Picrorhiza Kurrooa in terms of catalpol.

Pharmacology:

Some herbalists have described Picrorhiza kurroa as liver herb. Today we have estimated active constituents of the drug, which may be responsible for the hepatoprotective activity of the drug. Most of the studies have shown Picrorhiza kurroa extract (standardized to kutkin content) has potential hepatoprotective activity as compared to placebo.

- Kutkin from Picrorhiza kurrooa has shown significant curative activity in vitro in primary cultured rat hepatocytes against toxicity induced by thioacetamide, galactosamine, and carbon tetrachloride.

- Liver injury was induced in 16 mice by thrice-a-week injection of carbon tetrachloride (CCl4) for nine weeks. Eight of them were given daily feeding of Picrorhiza kurrooa extract (12 mg/Kg) 10 days prior to CCl4 injection. Control mice (n = 6) were injected with olive oil for the same period. Serum markers of liver injury and histology of liver tissues were studied. Hepatic glutathione, total thiol, glucose 6-phosphate dehydrogenase, catalase, lipid peroxidation and plasma membrane-bound Na+/K+ ATPase were also determined. The extract of Picrorhiza kurrooa appears to offer significant protection against liver damage by CCl4.

- In another study, the active constituent of Picrorhiza. kurrooa, showed a dose dependent hepatoprotective activity against oxytetracycline induced hepatic damage in rats.

- In a randomised, double-blind placebo controlled trial in patients diagnosed to have acute viral hepatitis, Picrorhiza kurrooa root powder 375 mg three times a day was given for 2 weeks or a matching placebo was given. Difference in values of bilirubin, SGOT and SGPT was significant between placebo and Pk groups.

Kutkin vs. silymarin:

Silymarin is a well-known hepatoprotective agent. Silymarin is a flavonol- lignan mixture obtained from seeds of Silybum marianum. Silymarin is a mixture of silybin, isosilybin, silychristin and silydianin. Silybin A and B are collectively known as silibinin. Randomized, controlled trials have proved efficacy of silymarin in liver diseases.

Picrorhiza kurroa, when compared with silymarin, the hepatoprotective effect of Picrorhiza kurroa was found to be similar, or in many cases, superior to the effect of Silybum marianum.

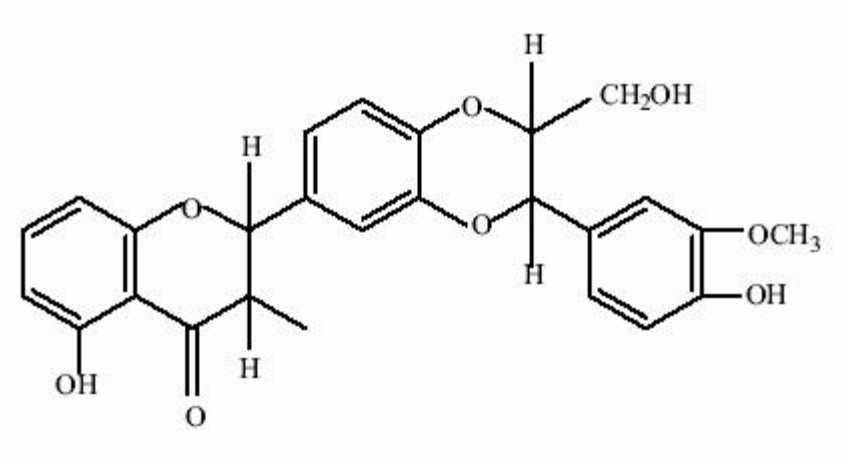


Fig 3: Structure of Silymarin

Mechanism of action:

The mechanism of action of Picrorhiza kurroa is not established.

The therapeutic activity of the drug may be based on two mechanisms:

1. Kutkins alter the structure of the outer membrane of the hepatocytes in such a way as to prevent penetration of the liver toxin into the interior of the cell.

2. Kutkins stimulate the action of nucleolar polymerase A, resulting in ribosomal protein synthesis and, thus stimulates the regenerative ability of the liver and formation of new hepatocytes.

3. Apocynin, is one of its constituents, has been found to exhibit powerful anti-inflammatory effects on a variety of inflammatory models.

Conclusion:

Mono- and polyherbal preparations with potent hepatoprotecive activity have been used in various liver disorders, More than 700 mono- and polyherbal preparations in the form of decoction, tincture, tablets and capsules from more than 100 plants are in clinical use. Silymarin has emerged as potential candidate with hepatoprotective agent. Kutkins have significant, even better hepatoprotective activity than silymarin and the drug should be screed for large-scale clinical trials.

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